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VALUE & OUTCOMES SPOTLIGHT

An HEOR news magazine

MOVING PATIENT CENTRICITY BEYOND TOKENISM:

JUST CHECKING THE BOX *MISSES THE POINT*

ISPOR

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The mission of *Value & Outcomes Spotlight* is to foster dialogue within the global health economics and outcomes research (HEOR) community by reviewing the impact of HEOR methodologies on health policy and healthcare delivery to ultimately improve decision making for health globally.

ISPOR
Improving healthcare decisions

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FROM THE EDITOR

More Than Slogans: Making Patient Centricity Real in Healthcare

"Patient centricity" seems to be a ubiquitous slogan in healthcare. It often appears in strategy documents, conference themes, regulatory guidance, corporate mission statements, and corporate responsibility. Yet its very popularity raises a critical question: Is patient centricity a substantive reorientation of healthcare around people's needs and values, or is it "tokenism," at risk of becoming an empty label attached to business as usual?

At its core, patient centricity refers to care that is respectful of and responsive to individual patient preferences, needs, and values, and decisions guided by those values. It implies a shift from a paternalistic model—in which clinicians and systems largely define problems and solutions—to a partnership model. In this view, patients are not passive recipients of services, but active participants in decisions, codesigners of services, and increasingly cocreators of research that informs clinical practice.

> Patient centricity involves organizing care and research around what matters most to patients, rather than around professional convenience, historical practice, or purely clinical endpoints.

Conceptually, patient centricity involves organizing care and research around what matters most to patients, rather than around professional convenience, historical practice, or purely clinical endpoints. This includes respect for individual preferences and values, shared decision making, and a holistic consideration of physical, psychological, and social well-being. It is no longer sufficient for systems, researchers, and payers to claim that patients are "at the center"; they are increasingly required to demonstrate how patients' preferences, experiences, and priorities shape evidence generation and decision making.

There are several pillars of this approach.

- Shared decision making is frequently described as foundational: Clinicians present options, clarify risks and benefits, and explore what matters most to the patient, aiming for a joint decision rather than unilateral prescribing.
- Patient-reported outcomes (PROs) and experiences extend this logic by systematically capturing symptoms, functional status, and perceptions of care directly from patients, and using those data to guide clinical decisions and evaluate performance.
- Codesign efforts seek to involve patients in planning care pathways, digital tools, and clinics themselves, to ensure services reflect lived realities rather than professional assumptions.

Evidence of impact is encouraging but nuanced. Studies of shared decision making and decision aids generally show improved knowledge, reduced decisional conflict, and, in some cases, better alignment between treatments and patient preferences.[1] Routine collection and use of PROs have been associated with improved symptom control, higher satisfaction, and even survival benefits in some oncology settings.[2] Interventions that support self-management and engagement often improve adherence to medications and lifestyle recommendations for chronic conditions.[3] However, effects on healthcare utilization and costs are mixed, and benefits are highly dependent on implementation quality.

Crucially, patient centricity is not merely about individual clinician behavior; it is a property of systems and organizations. Stress is placed on the importance of governance structures that include patient voices, metrics and incentives aligned with outcomes and experiences that matter to patients, and interdisciplinary teamwork that supports continuity and coordination of care. Digital tools—patient portals, telehealth, mobile apps, and remote monitoring—are often presented as enablers, providing greater access to information, communication, and self-management resources. At the same time, they raise concerns around usability, information overload, privacy, and the risk of exacerbating the digital divide.

As multiple articles in this issue of *Value & Outcomes Spotlight* suggest, governance and process changes are shaping a more patient-centric environment. Regulators and health technology assessment (HTA) agencies increasingly solicit structured patient input through submissions, advisory panels, and participation in committee deliberations. Patients are also engaged earlier in the research cycle, contributing to the definition of research questions, endpoint selection, and study design. Empirical studies indicate that such engagement can alter priorities, bringing under-recognized outcomes—like daily functioning or psychological impact—into sharper focus.

Despite progress, several gaps persist. Patient engagement and data collection often underrepresent marginalized or less-connected populations, raising concerns about equity and generalizability. Standardization of best practices for PROs, preference study design, and integration into economic models continues to evolve. Moreover, institutional incentives and decision frameworks may lag methodological advances, leading to situations where patient-focused evidence is generated but has limited influence on final coverage or pricing decisions.

Patient engagement and data collection often underrepresent marginalized or less-connected populations, raising concerns about equity and generalizability.

The gap between rhetoric and reality remains a central challenge. Many healthcare organizations endorse patient centricity in principle but struggle to embed it meaningfully in practice. Time pressures, workload, and reimbursement models that favor volume over deliberation are repeatedly cited as barriers. Clinicians may feel they are already working at capacity and see shared decision making or detailed explanations as aspirational but impractical for tightly scheduled appointments. Organizational cultures that value throughput and technical performance over listening and partnership can further limit progress.

Measurement is another tension point. Policy makers and payers increasingly rely on patient experience surveys and other metrics to assess and incentivize patient-centered care. While measurement can drive attention and accountability, it also risks reducing a complex concept to checklists and scores. Overemphasis on easily measured elements (for example, satisfaction with waiting times) may crowd out less tangible yet crucial aspects such as feeling heard, respected, and involved in decisions. There is an ongoing debate over how to capture what matters to patients without oversimplifying outcome measures or encouraging superficial compliance.

Equity concerns cut across all of this. Patient-centric approaches often assume a certain level of health literacy, confidence, and digital access. Without deliberate attention to inclusion, they may preferentially benefit those who are already better positioned to navigate healthcare—educated, affluent, digitally connected—while leaving behind people with language barriers, limited literacy, unstable housing, or distrust of institutions. Similarly, patient involvement in governance and research can devolve into tokenism if only a narrow, relatively privileged subset of patients is engaged and if their input has limited influence on decisions.

Overall, indications are that patient centricity is both an ethical imperative and a technical agenda. It requires rigorous methods for capturing patient experience and preferences, transparent incorporation of these data into economic evaluations, and governance

structures that give patients a meaningful role in shaping the evidence base. The field is moving from rhetoric toward implementation, but realizing the full potential of patient centricity will depend on sustained methodological innovation, inclusive engagement, and alignment of incentives across stakeholders—including patients.

The future of patient centricity will likely hinge on whether it can move from aspiration and rhetoric to grounded, equitable practice. That requires aligning payment and performance systems with patient-defined outcomes, investing in communication and health literacy, designing digital tools with and for diverse users, and sharing power with patients in governance and research. It also requires acknowledging trade-offs: authentic partnership can be time-consuming, uncomfortable, and occasionally at odds with efficiency metrics.

As a guiding principle, patient centricity retains strong intuitive and ethical appeal. The key test for health systems, professionals, and life-science organizations is whether they are prepared to redesign structures, workflows, and incentives to make it real—beyond slogans, checklists, and campaigns—especially for those patients who have historically waited longest for their voices to be heard.

As always, I welcome input from our readers.
Please feel free to email me at zeba.m.khan@hotmail.com.

Zeba M. Khan, RPh, PhD
Editor-in-Chief,
Value & Outcomes Spotlight

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FROM THE CEO

Moving From Aspirational to Operational Engagement of Patients in Healthcare Decisions

Rob Abbott, Chief Executive Officer, ISPOR

The management scholar, Peter Drucker, famously said, "Culture eats strategy for breakfast." His point was that ideas that seem obvious routinely fail because organizational culture prevents them from happening. I've been thinking about this in the context of healthcare because actively collaborating with patients as true partners seems intuitively obvious, and yet the reality is often little more than tokenism. The "culture" of healthcare ecosystems is eating the strategic idea of patient centricity for breakfast. We can do better. We *need* to do better.

This issue of *Value & Outcomes Spotlight* goes a long way toward answering the questions that lie at the heart of true patient centricity in healthcare. The papers collected here show how a mix of historical, structural, epistemic, and psychological factors has worked against meaningful integration of patients in healthcare decision making. Equally, they surface important ideas and use cases to demonstrate how these barriers can be overcome.

> We must resist the reflexive urge to rely solely on clinical or academic "experts" and listen to what patients actually value.

Everything ISPOR does is ultimately in service of patients and their caregivers, friends, and families. Our vision of a world in which healthcare is accessible, effective, efficient, and affordable for all speaks to our desire to ensure that people across the world have access to the care they need, when they need it, at a price they can afford. How can we deliver on that vision if we marginalize the patient voice? We must resist the reflexive urge to rely solely on clinical or academic "experts" and listen to what patients actually value. Better still, we must shift the role of the patient from a passive subject to an active partner in the clinical and research process.

Happily, ISPOR has already made some important progress in this regard:

- ISPOR views patient engagement as a collaborative partnership in which patients and researchers work together across all stages of the research process. This includes identifying research questions that are meaningful to patients, rather than just focusing on clinical metrics. This is hard to implement in practice because most clinical systems are designed around throughput—short appointments, productivity metrics, and standardized pathways. Still, we passionately believe that meaningful patient engagement requires taking the time to explain options, explore patient values, and thoughtfully deliberate about tradeoffs.
- The ISPOR Roadmap for Patient Preferences provides guidance on how to conduct studies that quantify what tradeoffs patients are willing to make (eg, accepting higher medical risks for better quality of life).
- ISPOR has developed—and continues to evolve—"Good Practices Reports" for using patient-reported outcome instruments. These are tools designed to capture a patient's health status directly from them, without interpretation by a clinician.
- ISPOR's Patient Council is a global body that serves as a strategic advisory group to the ISPOR Board of Directors, ensuring that patient perspectives are integrated into the Society's strategic initiatives, most notably our 2030 Strategy.
- For many years, ISPOR has convened patient roundtables in Europe, North America, Latin America, and the Asia-Pacific region to allow patient advocates to interact with other healthcare stakeholders like payers and manufacturers—and equally, to grow our own understanding of the issues that matter most to patients.
- ISPOR offers a specific membership category for patient representatives and provides travel grants to help them attend scientific conferences and share their expertise.

While the efforts mentioned above are encouraging, I would stress that healthcare systems as a whole are not yet ready to give patients a *central* role in value assessment. Progress is being made, and structural, methodological, and cultural barriers still limit full integration. While there are some encouraging case studies around the world, patient input too often supplements rather than drives value assessments.*

Why is that?
It is true that in some parts of the world, professional cultures still lean toward paternalism (the doctor knows best), and knowledge asymmetry makes engagement challenging and/or reduces it to consent versus collaboration. But perhaps the most important barrier is rooted in how reimbursement decisions are made. These decisions require consistent and comparable metrics and integrating qualitative patient insights

* The Patient-Centered Outcomes Research Institute (PCORI) in the United States requires patient engagement in funded research, and the National Institute for Health and Care Excellence in the United Kingdom includes patient testimonies and patient organization submissions in its appraisal processes. Canada's Drug Agency (formerly the Canadian Agency for Drugs and Technologies in Health) integrates patient input into drug reimbursement reviews.

into quantitative models is hard. At times it can seem like trying to fit the proverbial square peg in a round hole.

Health economic models rely heavily on measures such as quality-adjusted life years (QALYs) and standardized instruments such as EQ-5D.† While useful for comparability, these measures do not capture all aspects of the patient experience; they exclude treatment burden and social impacts; and they often simplify lived experience into a small number of domains.

So, how to move forward and ensure patient engagement goes beyond token participation?
We must move from symbolic inclusion or tokenism to meaningful partnership throughout the research life cycle. Tokenism is plainly evident when patients are consulted late, have little influence on decisions, or represent only a narrow patient voice. Among the steps that should be taken to make centricity a reality are:

- Identifying and engaging patients early in the research process. They should be shaping the research agenda and the questions to be answered
- Giving patients real decision-making roles
- Providing training and capacity building
- Compensating patients for their time and acknowledging their contributions in the same way we do for other "experts"

In view of ISPOR's (and HEOR's) focus on value, and our interest in expanding the definition of value to better reflect the things that matter most to patients, it seems only natural that we lean into all of the ways we might better integrate patients and their perspectives into health economics and outcomes research.

Traditionally, health economists have defined value based on clinical effectiveness and cost-effectiveness, as reflected in the oft-cited (and sometimes maligned) QALY. When patient experiences are incorporated into notions of value, the concept becomes broader, multidimensional, and more patient-centric. Suddenly, we lift our gaze from a singular focus on outcomes such as survival, disease progression, and clinical biomarkers to consider outcomes that matter in daily life, such as the ability to work or attend school, independence in daily activities, emotional well-being, and social participation—the simple, regular things that shape an individual's life.

> Value needs to shift from clinical efficacy alone to overall quality of life and functional improvement for patients. To get there, we need to put patients at the center of our thinking and decision making and cocreate the future together.

I think many of us in the health economics and outcomes research field know that value needs to shift from clinical efficacy alone to overall quality of life and functional improvement for patients. To get there, we need to put patients at the center of our thinking and decision making and cocreate the future together.

I'm proud of the work ISPOR has already done in this regard, and as your CEO, I pledge to keep pushing forward to ensure that we are genuinely moving from aspiration ("talking a good game") to operational engagement ("walking the talk").

† EQ-5D is a standardized self-report questionnaire designed by the EuroQol Group to measure health-related quality of life across 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It provides a simple, generic index for assessing patient health status and outcomes, and is routinely used in clinical trials and health economic evaluations.

ISPOR SPEAKS

From Aspiration to Action: Advancing Patient-Centered Evidence Globally at ISPOR

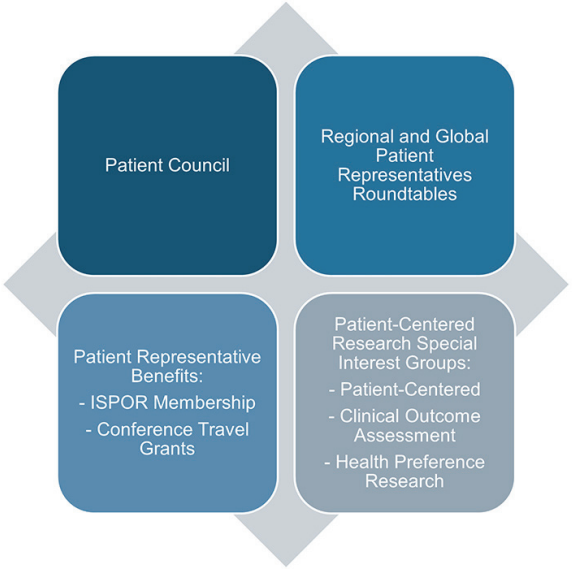
Clarissa Cooblall, MPH, Senior Director, Scientific Initiatives, ISPOR; **Sahar Alam, MPH**, Senior Manager, Scientific Initiatives, ISPOR

The landscape of healthcare research is evolving. Patients are not just subjects but active contributors, valued for their lived experiences, perspectives, and expertise. ISPOR—The Professional Society for Health Economics and Outcomes Research—is leading this transformation. It is redefining the role of patients in health economics and outcomes research (HEOR) through an ambitious and inclusive strategy for patient engagement and patient-centered evidence.

ISPOR envisions a global healthcare system where patients are not passive recipients of care but equal partners in shaping the policies, innovations, and research that affect their lives. ISPOR's longstanding commitment to elevating patient perspectives is based on the belief that meaningful and authentic patient involvement enhances the quality, relevance, and equity of healthcare solutions worldwide.

ISPOR's commitment to patient-centered evidence is operationalized through its Patient Engagement in HEOR Strategic Initiative (Figure 1), designed to make patient representatives cocreators, not just participants, of healthcare research and decision making.[1] This commitment is further underscored in the ISPOR Top 10 HEOR Trends,[2] which identifies patient centricity as a priority for 2026–2027. Complementing this, ISPOR's Good Practices Reports[3] demonstrate a sustained focus on patient-centered research, with nearly half of more than 75 published reports dedicated to this area, offering critical methodological guidance and advancing best practices in the field. ISPOR's HEOR by Topic page on Patient-Centered Research further amplifies this work by providing a centralized and comprehensive platform for knowledge, insights, and best practices.[4]

Figure 1. ISPOR Patient Engagement in HEOR Initiative



Defining Authentic Patient Engagement

In collaboration with academic and patient advocacy leaders, ISPOR has helped articulate a robust definition of "patient engagement in research": ***The active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners***.[5]

This definition emphasizes a transition from tokenistic patient involvement to genuine partnership. It is also actively applied across ISPOR's scientific activities, including conference and *Value in Health* submissions, where it guides expectations for meaningful patient engagement in research. The ISPOR Patient-Centered Special Interest Group is working to further evolve this definition to incorporate caregiver perspectives, reflecting a broader, more inclusive understanding of lived experience.

Despite growing recognition of its importance, challenges remain. Results from the "*ISPOR Membership Survey: Measuring and Evaluating the Quality of Patient Engagement Activities*" conducted by this Special Interest Group revealed a significant disconnect: While more than three-quarters of respondents identified their work as "patient-centered," fewer than half correctly aligned this with involving patients as partners in research, rather than only as study participants. This gap highlights the need for clearer frameworks, education, and standardized practices that promote authentic engagement.[6]

The ISPOR Patient-Centered Research Summit 2024

On May 5, 2024, ISPOR hosted its inaugural Patient-Centered Research Summit in Atlanta, Georgia, convening more than 200 participants from more than 20 countries, including patients, researchers, policy makers, industry leaders, and regulatory bodies. The Summit provided a global platform to celebrate progress, share best practices, and cocreate solutions for advancing patient-centered research. The key themes from the Summit are identified in **Table 1**.

Together, these insights highlight a clear path forward—one in which patient engagement is systematically embedded to strengthen the quality, relevance, and impact of HEOR.

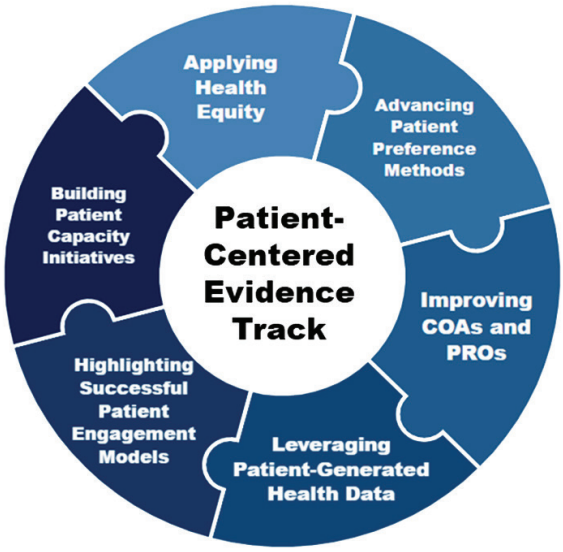
ISPOR Europe 2025: Patient-Centered Evidence Track

Building on this Summit and integrating the content in the full conference programming, ISPOR launched the Patient-Centered Evidence conference track at ISPOR Europe 2025. The track positioned patient engagement as a scientific standard, showcasing research cocreated with patients and integrating their voices throughout the HEOR process. These sessions recognized patients' expertise and lived experiences, demonstrating how collaboration enhanced the relevance, usability, and impact of research. Within this conference track,

Table 1. Key Themes from the ISPOR 2024 Patient-Centered Research Summit

THEME	INSIGHT	IMPLICATIONS FOR ACTION AND IMPACT
Trust and Equity	Meaningful patient engagement requires addressing persistent imbalances in access, representation, and opportunity.	Advancing inclusive and culturally responsive engagement approaches can improve representativeness, reduce bias, and strengthen the relevance of evidence across diverse populations.
Patient Leadership	Patients and patient organizations are increasingly influencing research priorities and regulatory discussions.	Integrating patients as partners in cocreation enhances the relevance, usability, and real-world applicability of research and decision making.
Global and Regional Innovation	Effective engagement strategies must reflect differences in healthcare systems, cultures, and resources.	Adapting models to local contexts supports broader global participation and strengthens the impact of patient-centered research across regions.
Standardization and Measurement	There is a growing need for consistent frameworks to define and evaluate patient engagement.	Applying standardized methodologies improves rigor, accountability, and the sustained integration of patient perspectives in health economics and outcomes research.

Figure 2. ISPOR Europe 2025 Patient-Centered Evidence Conference Track Priority Areas



COA indicates clinical outcome assessment; PRO, patient-reported outcome.

40% of submitted abstracts were identified as patient-centered. Additionally, 21% of all abstract submissions reported engaging with patients in the research process. The track highlighted cutting-edge research and case studies across several domains, identified in **Figure 2**.

Global Dialogue in Action: The ISPOR Global Patient Representatives Meeting

In January 2026, building on its patient engagement momentum, ISPOR convened 40 global leaders in patient-centered research from across the United States, Canada, Latin America, Europe, Asia-Pacific, and Africa. Discussions centered on embedding patient perspectives more systematically across the evidence ecosystem, with particular focus on the growing importance of patient experience data (PED). Participants examined emerging regulatory developments, including the reflection paper on PED from the European Medicines Agency (EMA), and explored how evolving expectations are shaping opportunities for sustained patient involvement in research, health technology assessment (HTA), and policy. Building on recent methodological advances, regulatory developments from EMA and the US Food and Drug Administration (FDA) emphasizing the importance of incorporating PED, and insights from this meeting, the ISPOR Patient Council will host a session at the upcoming ISPOR 2026 conference on *Advancing Patient Experience Data to Strengthen Patient-Centered Real-World Evidence*.

Capacity building was a key theme highlighted from participants at the Global Patient Representatives Meeting, with dialogue highlighting tools and strategies to strengthen patient representatives' roles throughout the research life cycle. The meeting generated actionable insights to inform ISPOR's evolving patient strategy, reinforced global collaboration, and underscored that lasting progress in HEOR depends on structured partnership and shared accountability.

The Future of Patient Partnership in HEOR

ISPOR continues to advance patient engagement in HEOR by actively gathering perspectives through dedicated events for patient representatives. By convening and engaging in interactive discussions, ISPOR creates opportunities for patients, researchers, and global stakeholders to share insights, highlight priorities, and identify barriers to meaningful participation. These dialogues inform and refine ISPOR's Patient Engagement in HEOR Strategic Initiative, ensuring that ISPOR's strategies and programs are grounded in real-world experiences and address the evolving needs of patients worldwide. Through this approach, ISPOR integrates diverse perspectives into its Patient Initiative, shaping a future where patient engagement is embedded at every stage of research and healthcare decision making.

In parallel, ISPOR actively engages with global decision makers and regulatory bodies, including the FDA and EMA, by contributing patient-informed perspectives to consultations and guidance development. This helps ensure that evolving regulatory and policy frameworks reflect real-world patient experience and priorities.[7-11]

As ISPOR looks to the years ahead, its commitment to elevating patient engagement and partnership is unwavering. A significant step in this direction is the addition of a question on patient engagement in the ISPOR conference submission process—an

initiative designed to elevate awareness of genuine patient-centered research and encourage researchers to actively involve patients as partners throughout the research life cycle.

This commitment is further reflected in the breadth of programming at ISPOR 2026, which will feature dedicated forums, such as *Collaborating With Patients to Define Digital Endpoints and Biomarkers That Truly Matter* and *Making Preferences Count: Patient Engaged Values Clarification for Individual-Level Decision Making*. Complementing these sessions, ISPOR will offer a short course on *Designing a Patient-Centered Strategy for Drug Development and Value*, as well as research poster tours focused on *PROs and Patient Preference*. These efforts are supported by the ISPOR Patient-Centered Research Topic, which highlights patient-centered research sessions across the conference and reinforces a structured approach to embedding patient perspectives in scientific research and evidence.

ISPOR's global commitment to patient-centered research aligns with the theme of the ISPOR Asia Pacific Summit 2026, "*The Future of Health Innovation: Unlocking Affordability and Access.*" Sessions will examine the expanding role of real-world evidence, artificial intelligence, and patient-centered research in informing evidence-based decision making, while addressing evolving definitions of value that integrate clinical, economic, and patient-experience perspectives. Individuals with ideas, comments, or an interest in helping define affordability from the patient perspective are encouraged to submit an abstract or reach out via email here.

ISPOR will continue to expand these efforts through initiatives such as the Patient-Centered Evidence conference track at ISPOR Europe 2026, with a focus on patient experience data. This track is dedicated to advancing the science of patient engagement by recognizing and leveraging patients' expertise, lived experiences, and knowledge to inform evidence generation.

Additionally, ISPOR's Strategic Plan 2030 focuses on a whole health approach and accounts for how patients define value considering their goals, preferences, and lived experiences. Whole health redefines value by placing patients and their families at the center, ensuring that outcomes, experiences, and priorities that matter most to them drive decision making and innovation.

Furthermore, patient-centered innovation empowers key stakeholders, including investors and early-stage innovators, to systematically engage with patients early. Translating patient insights into decision-relevant learning can inform strategy, strengthen evidence generation, and enhance long-term value creation. More about this topic will be covered at the ISPOR Healthcare Investment Summit 2026.

How to Get Involved

There are multiple avenues for individuals to engage with the ISPOR Patient Engagement in HEOR Strategic Initiative.

- Interested individuals from the global HEOR community are welcome to connect with the ISPOR Patient Council to learn more about ongoing initiatives and opportunities for collaboration and provide ideas and feedback on the Initiative.
- ISPOR also offers a range of engagement platforms, including patient-centered research Special Interest Groups (Clinical Outcome Assessment, Health Preference Research, and Patient-Centered), Task Force Review Groups, and patient-centered research Online Communities.
- In addition, ISPOR supports patient representative participation in its conferences through the ISPOR Patient Representative Travel Grants, with the next application cycle for ISPOR Europe 2026 opening in Summer 2026.
- Email patientcouncil@ispor.org with questions, comments, and ideas.

Together, these opportunities ensure that patient voices are meaningfully represented and integrated across ISPOR's scientific and collaborative activities.

Helpful Links and Resources:

- HEOR by Topic: Patient-Centered Research
- Special Interest Groups
- Strategic Initiative: Patient Engagement in HEOR
- Good Practices Reports & More
- Upcoming ISPOR Events

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HEOR NEWS

1 FDA Reminds Medical Companies and Researchers of Trial Results Transparency Requirements (FDA)

The US Food and Drug Administration has reminded more than 2200 medical product manufacturers and researchers to disclose clinical trial results—including unfavorable results—as required by law. According to an internal analysis, 29.6% of studies that are highly likely to fall under mandatory reporting requirements have no results submitted to the online database.
Read more.

2 Proposed 2027 US Budget Cuts $4.3 Billion for Global Health, Prioritizes Bilateral MOUs (Health Policy Watch)

US President Donald Trump's proposed 2027 budget will eliminate $4.3 billion for global health, including all funding for the Pan-American Health Organization and disease-specific State Department accounts like the US President's Emergency Plan for AIDS Relief. The budget calls for global health assistance to be contingent on bilateral memorandums of understanding (MOUs) with individual countries.
Read more.

3 Genetic Variants May Help Predict Weight Loss and Side Effects Associated With GLP1 Medications (Nature)

Genetic variants are associated with outcomes and adverse events in people taking glucagon-like peptide 1 (GLP1) receptor agonists for weight management, according to an analysis from the 23andMe Research Institute. The study identified 1 variant associated with increased weight loss efficacy and 2 variants associated with drug-related nausea or vomiting.
Read more.

4 Custom Offloading Footwear Cost-Effectively Help Prevent Diabetic Foot Ulcer Recurrence (Diabetologia)

Custom footwear designed to offload high pressure areas of the foot is cost-effective with high probability for helping to prevent foot ulcer recurrence in patients with diabetes, according to research from The Netherlands. The maximum probability for cost-effectiveness was 0.81 overall and 0.95 in the subgroup of patients who wore the footwear as prescribed.
Read more.

5 Model Finds 10-Year Outcomes Favor Stool-Based Colorectal Cancer Screening Over Colonoscopy (JME)

Cumulative screening effectiveness over 10 years is greater for stool-based colorectal cancer screening every 3 years than 1 colonoscopy, according to a model-based evaluation that incorporated real-world adherence data. Next-generation multitarget stool DNA testing was associated with greater colorectal cancer mortality reduction and 62% more life-years gained compared with colonoscopy.
Read more.

6 Cost-Effectiveness Study Supports Food Fortification to Address Global Dietary Deficits (The Lancet Global Health)

Large-scale food fortification (adding micronutrients to commonly consumed foods during processing) is a cost-effective intervention that greatly reduces nutritional deficiencies, according to an analysis that integrated modeled dietary data from the Global Dietary Database and fortification program parameters from the Global Fortification Data Exchange.
Read more.

7 Real-World Evidence Details Extent of Pandemic Blood Pressure Control Disruption (JAHA)

Blood pressure control rates were disrupted during the COVID-19 pandemic among patients with hypertension and had not fully rebounded by the end of 2022—a deficit that could adversely affect cardiovascular outcomes, according to a study that analyzed electronic health record data from the National Patient-Centered Clinical Research Network.
Read more.

8 Modeling Data Inform Swedish Decision to Implement National Chickenpox Vaccination (Acta Paediatrica)

Sweden's new national program for varicella (chickenpox) vaccination is predicted to result in both health gains and reduced costs from a societal perspective, according to a modeling study by the Public Health Agency of Sweden that informed the government's decision to approve the program. The predicted cost savings were primarily due to a reduction in caregiver productivity loss.
Read more.

9 Black Adults in Canada Report More Cost-Related Prescription Nonadherence Than White Adults (CMAJ)

Black adults in Canada are more likely than White adults to cite cost concerns as a reason for declining to fill a prescription or skipping doses, according to an analysis of person-level microdata from 5 cycles of the Canadian Community Health Survey. Having insurance coverage significantly reduced the rate of cost-related nonadherence among both Black and White adults.
Read more.

10 Cost-Effectiveness Drives Practice for Preventing Hospital-Acquired Infection (JAMA Network Open)

Cost-effectiveness consistently drives selection of infection prevention and control practices against hospital acquired infection, according to a survey conducted by researchers from Singapore. The survey, which included 256 health professionals from 6 global regions, found that implementation duration was the least important attribute across most regions.
Read more.

ISPOR NEWS

Advancement of Hepatitis C Elimination in the United States Earns Inaugural ISPOR Impact Award

Jagpreet Chhatwal, PhD, Mass General Brigham and Harvard Medical School, Boston, MA, and **Rachael Fleurence, PhD**, former Senior Advisor to National Institutes of Health Director and Senior Health Policy Advisor to the White House (currently with Apodexis Strategies, LLC, Bethesda, MD).

The ISPOR Impact Award established in 2025 recognizes health economics and outcomes research (HEOR) that measurably improves health and healthcare. The inaugural award honored Jagpreet Chhatwal and Rachael Fleurence for a multiyear collaboration that translated rigorous HEOR work into national policy action aimed at eliminating hepatitis C virus in the United States. Their work provided the quantitative backbone used for initial discussions at the White House to define the national hepatitis C elimination plan, and subsequently with the US Congressional Budget Office (CBO) to determine the potential budgetary impact of the "Cure Hepatitis C Act of 2025."

How It Started

The story behind the importance of this work and award starts in 2015, when highly effective direct-acting antivirals (DAAs) for hepatitis C arrived with cure rates near 95% but price tags of about $84,000 per treatment course. At that time, more than 3 million people were infected with HCV, the leading cause of hepatocellular carcinoma and the most common indication for liver transplantation. But despite the clear clinical benefit offered by DAAs, more than 35 state Medicaid programs severely restricted access, fearing budget blowouts. Chhatwal and colleagues published the first comprehensive cost-effectiveness and budget impact analysis, showing that DAAs were cost-effective even at premium prices, but raising tough questions about affordability and implementation at scale.[1]

That initial analysis did more than demonstrate good value. It framed the central policy paradox: How do we pay for cures today to avoid even greater downstream costs tomorrow? The work influenced payer–manufacturer negotiations, while also attracting broad media attention in outlets like the *Wall Street Journal* and Forbes. This early phase already encapsulated a core lesson of the award: HEOR has greatest impact when it explicitly addresses the decision context, not just the average cost per quality-adjusted life year.

Building Tools That Put Modeling Power in Policy Makers' Hands

Recognizing that journal articles alone could not meet the needs of policy makers in diverse health systems, Chhatwal's team invested in designing accessible decision-support platforms for both the United States and globally.

> Decision-support tools for stakeholders democratize the use of HEOR by removing the need for in-house modeling expertise while retaining methodological rigor.

The Hep C Calculator, developed with the World Health Organization, allows users in more than 28 countries—representing roughly 70% of the global hepatitis C burden—to input their own epidemiology and cost data, then immediately see cost-effectiveness outputs for alternative strategies.[2] Since its 2017 launch, it has directly supported price negotiations and treatment scale-up decisions in many middle- and low-income settings.

Next, in collaboration with the Centers for Disease Control & Prevention, the team developed The Hep C State Policy Simulator, which enables all 50 US states and the District of Columbia to model the epidemiologic and budgetary

Fleurence (left) and Collins (right) briefed President Joe Biden about the national hepatitis C elimination plan in September 2023.

Chhatwal (far right) attended a meeting on hepatitis C elimination at the White House in 2022.

consequences of policies such as universal screening, different treatment targets, or drug price scenarios tailored to each state's baseline burden and payer mix.

These tools democratize the use of HEOR by removing the need for in-house modeling expertise, while retaining methodological rigor. For state Medicaid programs and ministries of health, "running the model" becomes as simple as adjusting sliders, rather than commissioning a new analysis every time priorities shift. This approach also illustrates a powerful template for other disease areas to potentially build sharable, parameterized models that can be localized quickly for new stakeholders and settings.

From Feasibility Studies to the Cure Hepatitis C Act

The next chapter of the story involves key contributions from Fleurence, who served as Senior Advisor to Francis Collins, MD, PhD, Director of the National Institutes of Health and Acting Science Advisor to President Joe Biden. In 2023, she coauthored a *JAMA* perspective with Collins titled "A National Hepatitis C Elimination Program in the United States: A Historic Opportunity," which laid out a clear operational framework for elimination based on 3 pillars: accelerated screening, a federal subscription model for curative medicines, and widespread point-of-care diagnostics.[3] This article became a touchstone in Congressional hearings and helped shape the narrative that hepatitis C elimination is both morally urgent and fiscally responsible.

> By preventing downstream and related illnesses, the Cure Hepatitis C Act is projected to save $17.7 billion in healthcare spending, of which $12.2 billion would accrue to the federal government.

Fleurence worked with Chhatwal to adapt their models for the specific technical and political questions facing the White House and Congress, along with Josh Sharfstein, MD, and Risha Irvin, MD, from Johns Hopkins University. This partnership connected academic modeling with the realities of federal appropriations, program design, and regulatory timing.

Figure. Compared with the status quo, the initiative is projected to avert significant disease burden and add life years within 10 years.

This evidence base set the stage for the centerpiece of the impact story: the Cure Hepatitis C Act of 2025, bipartisan legislation introduced by Senators Bill Cassidy, MD, (R, Louisiana) and Chris Van Hollen (D, Maryland). The CBO relied directly on Chhatwal's National Bureau of Economic Research working paper (Projected Health Benefits and Health Care Savings from the United States National Hepatitis C Elimination Initiative[4]) to estimate the bill's fiscal effects. The modeling projected that a national elimination initiative could avert 20,000 cases of liver cancer, 49,000 cases of diabetes, 25,000 cases of chronic kidney disease, and 24,000 deaths, and add 220,000 life years within 10 years. By preventing downstream and related illnesses, the initiative is projected to save $17.7 billion in healthcare spending, of which $12.2 billion would accrue to the federal government.

> Combining rigorous modeling with strategic policy partnerships and user-centered tools can move evidence from journal pages to legislative text and, ultimately, to fewer preventable deaths.

The CBO's work was not just a technical exercise; it was essential for Congressional consideration of the Act. Throughout the process, Chhatwal, Sharfstein, Fleurence, and Irwin provided clarifications, scenario analyses, and technical consultation to align modeling assumptions with CBO's requirements. In this way, HEOR moved from the margins to the center of legislative deliberation, shaping legislators' understanding of the long-term budgetary implications of a "cure now, save later" strategy.

This work also provided important training opportunities for students and early career researchers to contribute to research with direct policy impact. Several trainees played key roles in the development and implementation of the hepatitis C models. In particular, Alec Aaron and Huaiyang Zhong interacted directly with the CBO, while Quishi Chen, Madeline Adee, and Yueran Zhuo contributed to earlier generations of the hepatitis C models that provided the foundation for the analyses used in the policy discussions.

At the same time, Fleurence helped coordinate the National Institute for Biomedical Imaging and Bioengineering (NIBIB)'s Rapid Acceleration of Diagnostics (RADx) program's collaboration with the US Food and Drug Administration (FDA) to address a critical bottleneck: lack of rapid, point-of-care hepatitis C RNA testing. In June 2024, FDA approved the first point-of-care hepatitis C RNA test in the United States. Here again, HEOR directly informed regulatory prioritization and underscored that access to diagnostics is as central to elimination as drug coverage.

The team's combined efforts extended to communication with state officials, international partners, and the public, and included White House briefings, technical consultations with Medicaid directors, and frequent media engagement on the promise and challenges of hepatitis C elimination.

Lessons Learned

Hepatitis C presented a paradox familiar to many payers: a curative therapy with compelling cost-effectiveness but high upfront costs and diffuse long-term benefits. Early responses focused on restricting access to protect short-term budgets, especially in Medicaid populations, prisons, and safety-net programs. This clash between clinical possibility and budgetary constraint created a unique opening for HEOR to redefine the policy conversation.

The work conducted by Chhatwal, Fleurence, and colleagues addressed this gap on several fronts. First, rigorous cost-effectiveness and budget impact models quantified how scaling up treatment would change infection rates, complication rates, and costs over decades, not just within one budget cycle. Second, the team translated these models into practical tools—the Hep C Calculator and the Hep C State Policy Simulator—that allowed policy makers to explore their own "what if" questions without needing to commission new analyses. Finally, they deliberately embedded this work in the policy process: adapting models for CBO scoring and informing White House deliberations.

Several lessons emerge for the HEOR community. One is that timing and format matter as much as methodological elegance: By working iteratively with policy makers, we ensured that the models answered the questions on the table and used inputs that agencies could recognize and trust. Another is that scalable impact often requires products, not just publications; interactive calculators and simulators can be reused, adapted, and localized far beyond the original study setting. A third lesson is the value of sustained engagement: over a decade of modeling, communication, and partnership laid the groundwork for the rapid uptake of the Cure Hepatitis C Act. For HEOR professionals working in other disease areas, this case suggests that combining rigorous modeling with strategic policy partnerships and user-centered tools can move evidence from journal pages to legislative text and, ultimately, to fewer preventable deaths.

Implications for Key Stakeholders

- *Policy makers*: For legislators and government agencies, this work illustrates how rigorous modeling can inform national strategies and budget decisions. Evidence-based policy frameworks can enable large-scale public health initiatives while ensuring fiscal sustainability.
- *Healthcare payers*: Economic analyses demonstrating long-term savings provide payers with the evidence needed to support broader access to curative therapies.
- *Public health agencies*: Interactive modeling tools empower health departments to tailor elimination strategies to local conditions and resource constraints.
- *Patients and advocacy groups*: Expanded screening and treatment access could prevent tens of thousands of premature deaths while dramatically reducing hepatitis C disease burden.

Acknowledgements: *The authors wish to thank Francis Collins, MD, PhD, former NIH Director and former Acting Science Advisor to the President; Josh Sharfstein, MD; and Risha Irvin, MD, who all played key roles in this endeavor.*

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ISPOR Events & Education

Use these quick links to learn more about ISPOR and the HEOR issues that matter most to you.

Resources for This Issue's Primary Theme

Patient-Centered Research: HEOR by Topic Page
Patient Centricity: Trend #6 in the 2026-2027 ISPOR Top Ten Trends
Patient-Centered Research: Topic Area for the ISPOR 2026 Conference Program
Patient Centricity: ISPOR Presentations Databases
Patient-Centered Research: An HEOR Competency (#12)
ISPOR's Patient Engagement Strategic Initiative
ISPOR Patient-Centered Special Interest Group

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Joint Clinical Assessment
PICO Scoping
Alzheimer Disease
Parkinson Disease
Neoantigen Therapy
Coverage with Evidence Development
Rare Diseases

POLICY BRIEF

The ISPOR Policy Brief offers concise insights into emerging developments in the global health policy space that shape access, innovation, and affordability. Each monthly installment spotlights timely issues with relevance for the health economics and outcomes research (HEOR) community and beyond, which provides readers with a rapid overview of how policy shifts are influencing global markets and stakeholders.

Pricing Reforms, Regulatory Shifts, and Global Market Reactions to Most Favored Nation

Ana Amaris, MD, MPH, Director, Health Policy Initiatives, ISPOR, Lawrenceville, NJ, USA

Overview: This March issue highlights several policy developments shaping the early months of 2026: initiatives affecting pharmaceutical pricing in the United States, regulatory changes related to evidence requirements for drug approval, and early international responses to US pricing policies. Together, these developments illustrate how governments and regulators are reassessing approaches to affordability, access, and innovation.

US UPDATES & PERSPECTIVES

ISPOR responds to GLOBE and GUARD
ISPOR submitted official commentary to the Centers for Medicare & Medicaid Services on the proposed GLOBE and GUARD models. These proposals signal a significant shift in US drug pricing policy, with implications for international reference pricing, methodological transparency, and the role of value in reimbursement decisions.

In our response, ISPOR emphasized the importance of methodological rigor, clarity in international price comparisons, and careful consideration of health system differences, fiscal contexts, and innovation incentives. The response underscored ISPOR's position that drug pricing reforms should be grounded in transparent, evidence-based approaches that support patient access while sustaining innovation.

The commentary reflects input from ISPOR's Health Policy leadership and members with expertise in health economics, outcomes research, and pricing policy.

Read ISPOR's full response here.

Debate emerges over codifying US Most-Favored-Nation drug pricing policy
The Trump administration has urged Congress to make its Most-Favored-Nation (MFN) drug pricing agreements with pharmaceutical manufacturers permanent through legislation, arguing that congressional action is needed to ensure the policy continues beyond the current administration. The agreements aim to reduce US drug prices by linking them more closely to prices paid in other high-income countries.

However, the support from Congress remains uncertain. Some Republican lawmakers and free-market groups have expressed concerns that a formalized policy could resemble government price controls, while industry stakeholders have opposed turning voluntary agreements into binding legislation.

TrumpRx platform shows limited early impact
One month after its launch, the Trump administration's drug discount platform, TrumpRx, appears to have limited scope and uncertain impact. The website lists only a small number of medicines (44 as of March 5th), and data on patient use and savings have not yet been publicly released.

The platform relies on voluntary agreements between the administration and pharmaceutical manufacturers to offer discounted prices on selected medicines. Analysts note that while the initiative could provide savings for some patients, its broader impact on overall drug spending will depend on whether more manufacturers and products are added to the program.

FDA signals shift away from 2-study requirement for drug approvals
The US Food and Drug Administration (FDA) plans to move away from its long-standing expectation that new drugs be supported by 2 clinical trials. Under the new approach, the agency's default position will allow approval based on a single pivotal study supported by additional evidence.

FDA leadership argues that advances in science and trial design allow regulators to determine effectiveness without requiring duplicate trials. The change is part of a broader effort to speed up drug development and regulatory review.

Single-trial approvals are already common for treatments targeting rare or life-threatening diseases. The new policy could expand this approach to drugs for more common conditions. Experts note that the impact will depend on how the FDA applies the new standard in practice.

INTERNATIONAL UPDATES

Nordic countries assess potential impact of US MFN drug pricing policy

Denmark and Sweden are evaluating the potential effects of the United States' MFN drug pricing policy, which aims to link US medicine prices to the lowest list price among comparable Organization for Economic Cooperation and Development countries. Both governments have launched analyses to assess possible implications for their pharmaceutical pricing systems and access to medicines.

Authorities in both countries note that the policy implementation remains unclear, and no concrete effects on drug access have been observed so far. However, policy makers and industry stakeholders have raised concerns that MFN could influence launch strategies for new medicines or reduce confidential price discounts for payers.

Recent developments in Denmark have further deepened these concerns. Amgen announced in February 2026 that it would withdraw its cholesterol-lowering medicine Repatha, (evolocumab), from the Danish market, citing changes in global pricing conditions. Some analysts have suggested that policies linking international prices could increase the risk that companies might delay launches or withdraw access to medicines in smaller-market MFN reference nations like Denmark to prevent negotiated discounts from affecting larger markets such as the United States.

Germany warns MFN uncertainty may delay drug launches

Concerns are emerging in Germany that uncertainty around the MFN drug pricing policy could begin to affect the launch of new medicines. In a recent interview with *Ärzte Zeitung*, VFA President Han Steutel noted that some companies are delaying or reconsidering product launches in Germany while they wait for greater clarity on how US pricing policies may evolve.

The issue comes amid broader debate about the financial sustainability of Germany's statutory health insurance system. A government-appointed Health Finance Commission is expected to present initial proposals by March 2026 to address rising health expenditures. Analysts note that additional pricing pressure, combined with uncertainty around international pricing policies, could increase the risk of delayed access to innovative medicines in the German market.

POLICY BRIEF

Early Global Responses to MFN Signal Shifts in Pricing and Access

Ana Amaris, MD, MPH, Director, Health Policy Initiatives, ISPOR, Lawrenceville, NJ, USA

Overview: This issue focuses on recent developments related to Most-Favored-Nation (MFN) drug pricing policies in the United States and their emerging global implications. It highlights how new policy tools, including trade-linked measures and institutional changes, are beginning to influence pricing strategies, industry behavior, and the broader policy environment.

US UPDATES & PERSPECTIVES

US Government Ties Pharmaceutical Tariffs to MFN Pricing and Domestic Manufacturing

The White House announced in early April the imposition of tariffs of up to 100% on imported patented pharmaceuticals and their ingredients, citing national security and supply chain resilience concerns.

The policy introduces a tiered tariff structure:

- 0% tariffs for companies that enter into MFN pricing agreements and commit to onshoring production and R&D
- 20% tariffs for companies with approved onshoring plans but no MFN agreement (increasing to 100% over time)
- 100% tariffs for companies that do not comply with MFN or domestic manufacturing expectations

Preferential rates apply under existing trade agreements, and several categories (including generics, orphan drugs, and certain specialty therapies) are exempt.

The measure explicitly frames pharmaceutical imports as a national security risk, positioning tariffs as a tool to incentivize both price alignment (via MFN) and domestic manufacturing capacity.

White House Proposes US Department of Health and Human Services (HHS) Restructuring, 340B Oversight Shift, and Support for Domestic Manufacturing

The Trump administration's proposed 2027 budget includes a 12.5% reduction in funding for HHS, alongside a broader reorganization of federal health agencies. The proposal would consolidate multiple entities—including the Health Resources and Services Administration (HRSA), the Office of the Assistant Secretary for Health, several centers and programs within the Centers for Disease Control and Prevention, and the Substance Abuse and Mental Health Services Administration—into a new entity, the Administration for a Healthy America.

The budget also proposes shifting oversight of the 340B Drug Pricing Program from the HRSA to the Centers for Medicare & Medicaid Services, citing the latter agency's greater in-house expertise in drug pricing and reimbursement.

In parallel, proposed provisions related to the US Food and Drug Administration aim to promote US-based drug development and manufacturing, including facilitating early stage clinical trials in the United States and strengthening the position of domestic manufacturers.

MFN Begins to Influence Pricing, Decision Making, and Global Policy Dynamics

Recent expert commentary suggests that MFN is evolving beyond a pricing proposal into a broader policy framework with real behavioral effects. Even in the absence of fully defined implementation mechanisms, the combination of pricing pressure, bilateral negotiations, and trade-linked incentives is already influencing manufacturer decisions on pricing, investment, and market strategy.

Some analyses raise fundamental questions about how drug prices should be determined under MFN approaches. By anchoring prices to external benchmarks, the policy risks shifting decision making away from value-based frameworks grounded in health technology assessment (HTA) and toward more mechanical forms of price convergence. This creates uncertainty around what constitutes a "fair" price in the US context and whether reliance on international references can substitute for domestically grounded value assessment.

From a global perspective, experts note that these dynamics may have broader implications for how value is defined and negotiated across health systems. As pricing becomes increasingly interdependent, the role of national HTA processes may be challenged by externally driven pressures, potentially reshaping both evidence expectations and access pathways.

INTERNATIONAL UPDATES

South Korea Advances Pricing Reforms While Navigating Global Pricing Exposure
South Korea, one of the reference countries considered in MFN pricing discussions, is advancing a broad reform of its pharmaceutical pricing system, with measures aimed at improving access to innovative therapies while tightening cost controls on generics and off-patent medicines.

Proposed changes include accelerated reimbursement timelines for rare disease treatments and expanded use of flexible pricing agreements alongside reductions in reimbursement levels for generics. While the reforms seek to rebalance incentives toward innovation and system sustainability, analysts warn that the changes may introduce market instability, particularly for manufacturers facing increased pricing pressure in the off-patent segment.

Manufacturers Delay European Launches as MFN Influences Global Strategies
Pharmaceutical companies are increasingly delaying or reconsidering the launch of new medicines in European markets, citing uncertainty related to US pricing reforms under MFN policies, as shown in recent reports. Industry data indicate a decline in European drug launches as manufacturers seek to avoid lower-priced markets that could influence US pricing benchmarks.

There are growing indications of fewer early access applications and delayed market entry decisions, reflecting concerns that US pricing policies may influence global launch sequencing and contribute to delayed access in lower-priced markets.

Japanese Pharmaceutical Companies Face Pricing Pressures Amid Policy Shifts
Japanese pharmaceutical companies, including major players such as Astellas, are navigating increasing pricing pressures both domestically and internationally. Ongoing reforms in Japan's pricing system, combined with global shifts in pricing expectations, are contributing to a more challenging commercial environment for innovative medicines.

These developments highlight broader concerns about the sustainability of current pricing models and the potential for global policy changes, including those originating in the United States, to influence pricing strategies and investment decisions across markets.

METHODS EXPLAINED

Metamodeling in Health Economics and Outcomes Research

Section Editor: **Koen Degeling, PhD**

What is Metamodeling?

Metamodels are models of existing models and are also known as surrogate models or emulators. A metamodel approximates the outcomes that an existing target model or "simulator" would produce based on a set of input parameters (**Figure 1**). In doing so, the metamodel provides a fast approximation of a model that may be too computationally complex (ie, slow) to use itself.

What Can It Be Used For?

In general, metamodeling is useful for 2 types of applications. The first is simulation modeling, where metamodels are used to reduce the computational burden of complex models or analyses. The second is statistical modeling, where metamodels are used to improve understanding of the target model by analyzing statistical relationships between model inputs and outputs.

In health economics and outcomes research (HEOR), the simulation objective is typically the most relevant and the focus of this article. In this context, metamodeling typically applies to cost-effectiveness models and the analyses that are performed with them. The motivation to use metamodels herein is to reduce the time needed to perform analyses that are computationally demanding either because the model itself is complex (eg, when using an individual-level simulation) or because the analyses require a model to be evaluated a large number of times. Key use cases include performing probabilistic (scenario) analyses or value of information analyses, or applying calibration or optimization algorithms.

How Does It Work?

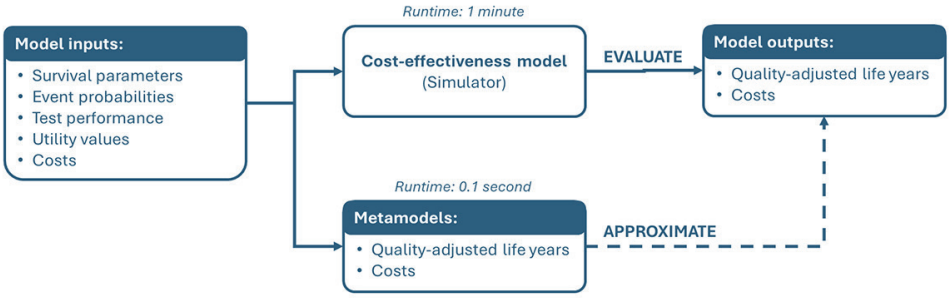
Metamodeling reduces computational burden by replacing the target model in analyses with rapid predictions from the metamodel. A wide range of techniques can be used to develop metamodels. In its simplest form, a metamodel can be a simple linear regression model fitted to the target model's inputs and outputs. More flexible regression approaches, including splines or generalized additive models, can be used to capture smooth nonlinear relationships. When the relationship between inputs and outputs is highly complex, machine-learning methods such as random forests, gradient boosting, or neural networks may be appropriate. Gaussian process emulators can also be used, particularly when training datasets are relatively small.

What Makes It Different From Other Modeling Methods?

Metamodeling is different from other modeling approaches commonly used in HEOR in that it requires an existing target model or "simulator" to be available. A metamodel cannot be developed in isolation, and its validity depends on the validity of the model it approximates.

Conceptually, the process of metamodeling resembles statistical modeling: A dataset is generated, a model is fitted, and predictive performance is assessed. The key difference is that, in metamodeling, the dataset is simulated from the target model rather than observed in real-world data. These simulated data are generated under a controlled experimental design. As a result, they are not affected by measurement error or confounding, which are typical for empirical datasets. Therefore, metamodels can achieve very high predictive accuracy.

Figure 1. Conceptual illustration of metamodeling based on Degeling et al.[1]
A computationally demanding target model maps input parameters (eg, clinical and economic parameters) to model outputs (eg, costs and quality-adjusted life years). A metamodel is fitted to input-output pairs generated from the target model and can subsequently be used to rapidly approximate model outcomes for new input combinations.



What Are the Steps in Applying Metamodeling?

A structured approach to metamodeling in HEOR is provided by the 6-step process (**Figure 2**) described by Degeling et al.[1] An essential prerequisite is the availability of a validated target model that is considered fit for purpose, because a metamodel

can never compensate for shortcomings in the original model. Note that most techniques require a different metamodel to be developed for each outcome. Correlation between outcomes can be accounted for using multivariate techniques or by including certain outcomes as predictors for other outcomes in a step-wise approach.

Step 1 – Identify one or multiple suitable metamodeling techniques based on the types and number of input and output parameters.

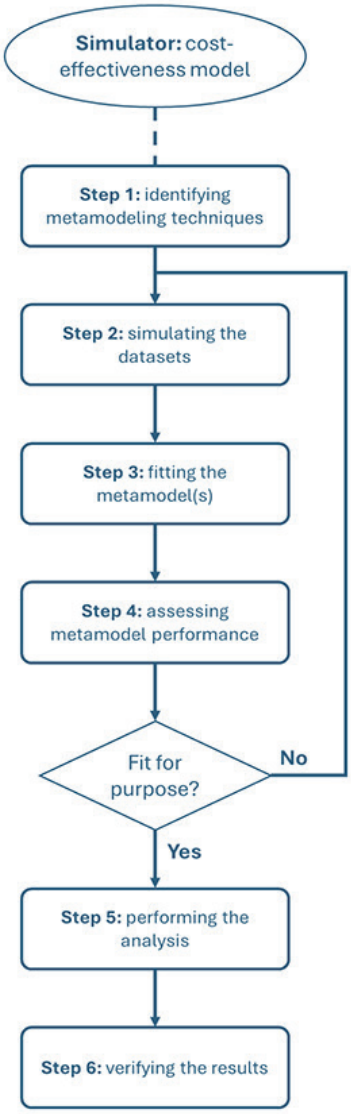
Step 2 – Simulate datasets for training and testing the metamodel(s) using the existing target model based on defined parameter ranges, preferably using an efficient design of experiments.

Step 3 – Fit the metamodel using the chosen technique based on the simulated training dataset.

Step 4 – Assess metamodel(s) performance on the simulated testing dataset using metrics that are relevant for the intended decision problem.

Step 5 – Conduct the required analysis using the metamodel(s) to reduce the runtime.

Figure 2. Simplified overview of the 6 steps involved in applying metamodeling to health economic models based on Degeling et al.[1]



Step 6 – Verify whether the results obtained with the metamodel(s) are consistent with the original target model.

There are also some areas where caution is needed when developing and using metamodels. First, metamodels make it easy to explore alternative scenarios, including scenarios beyond the evidence base for which the target model was developed and validated. This effectively constitutes a form of extrapolation that should be performed with caution. Second, the value of a metamodel depends on its validation, which should be performed with care. Computational efficiency should not come at the expense of confidence in the outcomes obtained.

In terms of software, metamodels in HEOR mostly have been developed in R, reflecting the availability of tools for design of experiments, regression and machine learning, and advanced analyses such as value of information analysis. However, metamodels can also be developed in R when the target models have been implemented in other software, such as Microsoft Excel.

What Is the Current Level of Adoption of Metamodeling in HEOR?

Metamodels are widely used in fields such as engineering and environmental modeling, where high-fidelity simulators are computationally expensive. In HEOR, however, applications remain relatively limited and are still more common in academic work than in routine health technology assessment (HTA) submissions.

Nevertheless, there are impactful examples demonstrating its value. The Sheffield Accelerated Value of Information (SAVI) tool,[2] for example, uses metamodeling to enable rapid estimation of value of information analyses from probabilistic analysis output.

Uptake of metamodeling may increase further as cost-effectiveness models continue to become more complex and as computationally demanding analyses are increasingly part of HTA guidelines. This includes probabilistic analyses and value of information analyses that are now mandatory in some jurisdictions.

An important area of further development is developing clearer guidance on validation standards, with emphasis on decision-relevant accuracy, also to support the assessments of metamodels by others.

What Are Some Key Resources for Further Reading?

For readers interested in a detailed methodological overview, the structured introduction by Degeling et al provides a starting point.[1] An applied example by Koffijberg et al illustrates the use of metamodeling to facilitate optimization of colorectal cancer screening strategies.[3]

Did you enjoy reading this article? Or do you have suggestions to improve the section or methods we should cover in future editions? Please share your feedback with the Value & Outcomes Spotlight *Editorial Office at voseditor@ispor.org.*

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MOVING PATIENT CENTRICITY BEYOND TOKENISM: JUST CHECKING THE BOX MISSES THE POINT

What patients want from healthcare interventions—and, importantly, what they don't want—have become indispensable factors in assessing the value of those measures. HEOR experts are supporting the thoughtful incorporation of patients' voices across the healthcare landscape as part of a movement toward inclusion of patients as research partners.

By Beth Fand Incollingo

Several decades ago, insights from patients about the level of symptom relief that would have a meaningful impact on their quality of life, or whether the clinical benefits of specific medical interventions outweighed the side effects, were considered "nice to have" by healthcare stakeholders. Now, that type of patient feedback—and tools for quantifying it—has become expected, if not essential, across drug development and the healthcare system.

"If a patient can't tolerate the drug, are they going to stay on it, or are they going to skip doses? When you're not considering a drug's impact on patients in their day-to-day lives, you greatly limit the ability to produce therapies that are effective from the patient's perspective," said Stacie Hudgens, Chief Scientific and Strategy Officer at Clinical Outcomes Solutions, which conducts research and incorporates patient insights across drug development.

The movement toward patient-centric healthcare dates back to the activism that brought patient advocates in contact with regulators during the AIDS crisis of the 1980s and 1990s, but it truly took root in the 2010s.

FROM THE PATIENT

"Patients do not experience their health in isolated variables. We experience it as a whole life."

—Lara Bloom

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That was when the United States Food and Drug Administration (FDA) launched the Patient-Focused Drug Development Initiative (PFDD)[1] and the 21st Century Cures Act, both of which required regulators to incorporate patient insights when issuing guidance or making decisions about drug development. As regulatory bodies across the world passed similar initiatives, the World Health Organization adopted a Framework on Integrated, People-Centered Health Services that encouraged national health systems to not just treat patients, but partner with them.[2]

Most recently, regulatory bodies in the United States, the United Kingdom, Canada, the Asia-Pacific region, and beyond have created and refined guidances for patient engagement,[3] Hudgens said.

As a result, she said, today's healthcare stakeholders—from drug developers and payers to health technology assessment (HTA) bodies and healthcare systems—would be hard-pressed to make a major decision without considering patient input.

The health economics and outcomes research (HEOR) community is uniquely positioned to amplify the impact of patient engagement by developing scientifically sound ways to gather insights, translating those findings into evidence about value, integrating the data into supporting materials, and ensuring that the information makes it to the desks of decision makers. At the same time, HEOR professionals are sharing best practices aimed at shaping and encouraging this kind of research.

"Across diseases and measurement approaches," Hudgens said, "the concept is the same: In addition to data on efficacy, safety, and tolerability, we need really good measurement validity evidence reflecting the patient voice. To me, that voice is the patient in their universe—school, work, home, family, friends. Our job is to capture that experience as perfectly as we can, interpret it, and put it forward on their behalf in clinical research."

With Patient Engagement, Health Interventions Gain Value

In recognizing patient centricity among its Top 10 HEOR Trends for 2026-2027, ISPOR noted that the approach is shaping the healthcare market.

ISPOR defines patient centricity as "the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise."[4]

Patient centricity adds to an intervention's value for every stakeholder across healthcare, including patients, pharmaceutical companies, physicians, health systems, regulators, and payers, Hudgens said.

Many organizations have recognized that by redefining value in healthcare to include the benefits of patient engagement—among them ISPOR, through frameworks including its Value Flower,[5] and the Institute for Clinical and Economic Review (ICER), which emphasizes patients' top concerns in its decisions about the cost-effectiveness of treatments in the United States.

An early example of patient insights supporting value was Viagra (sildenafil), a modestly effective cardiovascular drug that became a blockbuster treatment for erectile dysfunction after Pfizer listened to patients when they said they didn't want to stop the medication.[6]

On the other hand, Pfizer's experience with Exubera exemplified what can go wrong when patients' needs aren't fully understood. Pfizer withdrew the inhaled insulin treatment for diabetes after a year on the market, at a $2.8 billion loss, because patients found its dosing complicated, its delivery system unwieldy, and its pulmonary side effects concerning.[7]

Another drug, Lotronex (alosetron), was pulled from the market by GlaxoSmithKline in 2000, only to return 2 years

later, after patients with treatment-resistant severe, diarrhea-predominant irritable bowel syndrome said it was the only therapy that had worked for their debilitating condition.[8]

While HEOR efforts don't always come with that much fanfare, the field's successes can change healthcare strategy in ways that boost patient engagement.[9]

FROM THE PATIENT

"Behind every data point is a person navigating their own reality. No 2 journeys are the same."

— Joslyn Chaiprasert-Paguio

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Hudgens is proud to have gathered patient insights in support of a New Drug Application for the prostate cancer treatment Erleada (apalutamide), because the FDA's review of the drug was the first ever made entirely available online.[10]

Transparency is also at the heart of Project Patient Voice, sponsored by the FDA's Oncology Center of Excellence, which publicly shares patient-reported outcomes from cancer clinical trials to facilitate decision making not only for drug developers, but for patients.

"I call that a win for healthcare and a win for HEOR," Hudgens said.

Moving Beyond Token Participation

To be meaningful, patient engagement must amount to more than an ethical goal or a token gesture, and progress in that area is still uneven, said Dalma Hosszú, Head of Patient Centricity and Engagement at the Syreon Research Institute in Budapest, Hungary, which supports healthcare decision making, and a Board Member focused on patient centricity for the Hungarian Health Economics Association.

"The mindset is shifting, but there are still structural barriers, such as lack of clear methodologies, limited capacity, or uncertainty about how to use patient input in a consistent and decision-relevant way," Hosszú said.

The single best way to improve that landscape, experts agree, is to consult patients from the very start of the process, from clinical trials to real-world studies and from the doctor's office to regulatory settings.

Stakeholders should notify patients early about opportunities, arrange ongoing commitments with them, and determine which situations call for early insights versus more rigorous studies, said Elisabeth Oehrlein, PhD, MS, founder and CEO of AppliedPX, a patient engagement research firm that focuses on collecting patient experience data and helping stakeholders use it to guide decisions across the product lifecycle.

Working with people who have direct lived experience can be especially helpful when you want to understand what it actually feels like to go through something, day-to-day realities, specific pain points, and the decisions people make, since they can speak to what has or hasn't worked for them in their own lives. Advocates, meanwhile, can offer a broader view by drawing on many voices, helping to identify patterns, common unmet needs, and system-level gaps, which can be useful when shaping strategy, setting priorities, or understanding the wider landscape. A great example is REMEDi4All, the European platform for drug repurposing, which "places the patient's voice and lived experience at the center of each project and promotes a model where patients are involved throughout the process," Hosszú said.

Guidance for accomplishing that goal, she noted, was offered in a recent study that identified 12 recommendations for "meaningful, systematic, and sustainable patient involvement" in HTA in Central and Eastern European countries.[11]

All those methods will gain value if stakeholders include insights from patients across socioeconomic backgrounds, said Alan Balch, PhD, CEO of the Patient Advocate Foundation (PAF), which provides direct assistance to US patients, and its global policy and advocacy arm, the National Patient Advocate Foundation. That's because low- and middle-income individuals, while often overlooked in research, have important information to contribute about the barriers they face related to managing their health, Balch said.

FROM THE PATIENT

"When patients are not included, studies can be technically strong but miss what matters."

—David Kelly

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Those issues may include problems affording treatment, an inability to take time off from work, inadequate childcare or transportation, or even a lack of reliable refrigeration for drugs that must be kept cool, he said.

To establish true, comprehensive patient centricity, Oehrlein said, "those of us in HEOR need to upskill in terms of understanding what constitutes meaningful engagement, and then what opportunities exist to use patient input across processes. A lot of this already exists, but we need to bring it to new stakeholders."

A Guide to Patient Engagement
Among the tools designed to support HEOR professionals in that endeavor are patient experience data dossiers.[12] AppliedPX and partners propose that these would give advocacy groups a template for collating data collected from patients and sharing the information with decision makers across a host of disease states.

"It would reduce the burden on patient groups and would be easier for decision makers to learn about patient experiences and integrate them into the decisions they need to make," Oehrlein said.

Another tool, standardized by Health Technology Assessment International, is already in use in Scotland, the United Kingdom, Australia, and Taiwan: plain-language summaries of evidence, culled from value dossiers.[13]

"These prime patients to participate and provide meaningful input," Oehrlein said.

FROM THE PATIENT

"Sometimes patient voices are invited to the table but not fully integrated into decisions."

—Kevin Wake

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In a previous role with the National Health Council, Oehrlein helped design a Patient Experience Mapping Toolbox—now being applied across numerous disease states—that can be adapted for different uses so that HEOR professionals don't have to rewrite discussion guides and redesign consent forms for every project.

The nonprofit Center for Innovation & Value Research contributed to the conversation in February 2026, when it published a Rare Disease Patient Engagement Guidance and Checklist to help rare-disease researchers boost patient involvement from the beginning to the end of the process.

Additional strategies are being developed by organizations central to patient engagement efforts, including the US-centric, nonprofit Patient Centered Outcomes Research Institute; the public-private European Innovative Health Initiative; and the International Society for Quality of Life Research.

ISPOR serves as a hub for the movement by modeling the importance of patient engagement, defining its standards, and providing tools for its implementation through:

- The society's Patient Council chaired by Balch
- Roundtable strategy discussions
- A Patient-Centered Special Interest Group
- Themed sessions at annual conferences
- A dedicated Research Summit; and
- Other educational events

"We're showcasing true patient-engaged science, patient-centered evidence, and patient involvement in the process," Balch said. "The response from the ISPOR community has been amazing."

Measuring Patient Insights
But how do HEOR professionals turn patients' lived experiences into metrics that can be scientifically analyzed and modeled?

The first step is to search for existing patient-reported outcomes tools, such as the Numeric Rating Scale for pain, although such instruments are often insufficient—especially when a study involves a rare disease. In those cases, Hudgens said, researchers must figure out what kinds of measures to introduce instead.

They can do that by hosting interviews and focus groups or conducting patient preference studies, which poll people about the risks they're willing to accept when receiving an intervention. For instance, Balch said, patients with prostate cancer may be willing to experience pain but not lose their sexual function, while those with breast cancer may be willing to live with nausea but not hair loss, as that could frighten their children.

Based on those findings, researchers must either adapt existing instruments or develop new ones. The resulting tools might measure the change in a symptom's severity or the proportion of patients who achieve a specific outcome, and they can be included in clinical trials as endpoints.

Another good strategy is to interview participants about their symptoms and functionality at both the beginning and end of a clinical trial, which can help determine whether positive clinical outcomes align with changes patients consider meaningful. For instance, a clinically significant improvement in fingernail psoriasis may vary between patients. It may be for one patient that they are able to resume working at a computer where this may not be the case for another patient, Hudgens said.

"Known as anchor items or global impressions of change, these global items can provide evidence to aid in the interpretation of COA endpoints, thus contributing to a drug approval by making findings interpretable," she said. "They (trial interviews) contextualize what is normally very dry, quantitative data by enhancing it with the patient voice."

An example is the label for Xermelo (telotristat ethyl), a treatment for carcinoid syndrome diarrhea, which not only describes a statistically significant decline in bowel movement frequency associated with the drug but also delineates the proportion of study participants who experienced a reduction they deemed meaningful, Hudgens said.[14]

Also valuable is goal attainment scaling, which enables patients in a clinical trial to define their own individual outcome goals but uses standardized scoring metrics to measure their results.[15]

Ultimately, Balch said, it will be up to the HEOR community to carve out a bigger role for patient engagement, not only in qualitative and anecdotal settings, but in HTA and other quantitative assessments.

"There are already ways to engage patients in the procedure and process, but where there's new opportunity is on the science side," he said. "The health economics community shapes the science, and ISPOR will play an important role in helping to advance it in ways that could be fruitful for HTA."

When Using AI, Caution Is the Watchword

In this technological age, artificial intelligence (AI) seems poised to help drive patient engagement.

"AI can play an important role in scaling patient engagement, especially when it comes to analyzing large datasets and identifying patterns across patient experiences and clinical research," said Hosszú, who pointed to a study that used the technology to identify the patient-reported outcomes implemented across a host of lymphoma clinical trials.[16] She added that AI is being deployed by the European Atlas on Clinical Trials in Cancer and Hematology to determine the availability of trials across Europe and the kinds of patient engagement tools they incorporate.

FROM THE PATIENT

"Our focus is ensuring evidence reflects real patient priorities and informs better decisions."

— Angie van Bemden

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Oehrlein uses AI to translate research questions into plain language for patients and Hudgens helped her company develop COAscape AI, which scrubs personal information from qualitative literature and analyzes it to help HEOR experts establish conceptual frameworks.[17]

"Our software uses the finite world of real data, so we can always go back to the source data and check whether the AI analysis got it right," Hudgens said.

What worries the experts is the idea of using AI large-language models to search the entire online universe or directly engage patients.

"That's not real data, it doesn't leave any audit trail, and it isn't specific enough," Hudgens said. "To me, you can never stop talking to patients."

Oehrlein agreed and emphasized the importance of verifying who is contributing to patient engagement research, as this directly affects the trustworthiness and quality of the data. Without that clarity, it becomes harder to know how much confidence to place in the findings.

"We always do a confirmation of diagnosis to make sure that the people we interview actually have the disease we're talking about," she said. "It takes more time and costs more money, but I don't know how else we can make sure these data are useful for decision making."

Balch has an additional concern: that AI, having only the information available online to interrogate, will replicate the existing research bias against low- and middle-income patients.

He's excited, though, about what he considers a more appropriate function for AI: assisting PAF in operating its directory of safety-net resources for patients in the United States by collecting basic information about applicants, matching them with programs for which they are likely eligible, and helping them apply.

"AI can understand the nuances of questions and where people get tripped up," Balch said. "That's important, because if you answer the wrong way, you may be denied, and once you're denied, you may not be able to reapply."

Moving Forward With Patient Centricity

To fully realize patient engagement, healthcare stakeholders and the HEOR experts who support them must move from isolated examples of good practice to systematic implementation, Hosszú said.

"We already have strong methodologies and growing experience, but these need to be embedded into standard processes and supported by clear guidance, resources, and incentives," she said. "At the same time, patient experience needs to be more consistently integrated into value assessment frameworks, so that it directly influences decisions—not just as supportive evidence, but as a core component of value."

Hudgens added that each of us should recognize our personal stake in patient centricity.

"At some time in our lives, everybody will be a patient, and probably also a caregiver," she said. "Because of that, we really have to think of everything from a patient-centered focus, because we would want the same thing for ourselves."

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FROM THE PATIENT

In keeping with the theme of patient centricity, this issue of Value & Outcomes Spotlight *is packed with insights from health economics and outcomes research (HEOR) experts and patient advocates about the importance of involving patients in all aspects of developing health technologies. But the real experts on this topic are the patients themselves. That's why we've asked 5 remarkable individuals to share their real-world perspectives as patients, patient advocates, and patient partners in healthcare research.*

"Patients Do Not Experience Their Health in Isolated Variables. We Experience It as a Whole Life."

Lara Bloom
President and CEO, The Ehlers-Danlos Society

How did you become involved in advocating for and/or participating in patient-centric outcomes research?
My journey into patient-centric outcomes research was never a career decision in the traditional sense. It was a necessity. Living with a complex, often misunderstood condition meant I quickly saw the gap between what mattered to clinicians and what shaped my daily reality. I stepped into advocacy to close that gap. Over time, that grew into working alongside researchers, not just as a subject, but as a partner. I have always believed that lived experience is not anecdotal. It is data with depth, and it deserves a seat at every table where decisions are made.

What's been the most rewarding thing for you about being a patient expert?
The most rewarding part has been seeing the patient voice move from the margins into the center of conversations. When a researcher pauses and says, "I had not thought of it that way," or when a study design shifts because of patient input, that is powerful. It means we are not just being heard, we are shaping outcomes. On a human level, it is also deeply meaningful to know that lived experience can create a smoother path for those who come after us.

What's been the most challenging thing?
One of the hardest things is the constant need to justify the value of lived experience. Patients are still too often invited in as a token rather than trusted as experts. There is also an emotional cost. You are not just sharing ideas, you are sharing pieces of your life, sometimes repeatedly, sometimes in rooms that are not yet ready to truly listen. Balancing that vulnerability with the need to remain strategic and impactful can be exhausting, but it is also what drives meaningful change.

What's something that research too often overlooks or gets wrong about what's important to patients?
Research too often focuses on what is easy to measure rather than what actually matters. Clinical endpoints might look neat on paper, but they rarely capture the full picture of living with a condition. Things like fatigue, cognitive load, social participation, and the ability to live with dignity are frequently overlooked.

Patients do not experience their health in isolated variables. We experience it as a whole life. When research misses that, it risks producing outcomes that look successful but feel disconnected from reality.

HEOR often involves assessing costs vs benefits of treatments. In your opinion, what is one type of cost and one type of benefit that aren't considered often enough in these analyses?
A cost that is often overlooked is the personal and societal impact of lost participation. When people cannot work, study, or engage in their communities, the ripple effects are profound, both economically and emotionally.

On the benefit side, we rarely measure restored quality of life in a meaningful way. Not just symptom reduction, but the ability to show up as a parent, a partner, a professional, or simply as oneself. Those are the outcomes that define whether a treatment truly makes a difference.

Lara Bloom is the President & CEO of The Ehlers-Danlos Society and an Academic Affiliate Professor of Practice in Patient Engagement and Global Collaboration at the Pennsylvania State College of Medicine. Based in the United Kingdom, she is a global leader in advancing patient-centered research, care, and policy for rare and chronic conditions.

FROM THE PATIENT

"Behind Every Data Point Is a Person Navigating Their Own Reality. No 2 Journeys Are the Same."

Joslyn Chaiprasert-Paguio
Cervivor Ambassador and Podcast Host

How did you become involved in advocating for and/or participating in patient-centric outcomes research?
After my most recent recurrence of cervical cancer in 2021, it hit me that while science has advanced in both diagnosis and treatment, there was still a significant gap in patient knowledge. Despite the human papillomavirus (HPV) vaccine and early detection, the number of deaths from cervical cancer was increasing. My dear friend, Tamika Felder, started Cervivor, a patient advocacy group with a mission to empower those affected by cervical cancer to help spread awareness and influence change. I wanted to get involved and use my voice to help others, which led me to begin hosting the Cervivor Podcast.

What's been the most rewarding thing for you about being a patient expert?
Part of being a patient advocate is sharing your story. Sometimes it can be triggering; other times, it creates a meaningful connection that may even change a life. Those moments of connection are truly the most rewarding part. Whether it's hearing a mom say she will vaccinate her child against HPV or receiving feedback from a clinician who will remember my story when talking to patients about cervical cancer, those are the moments that make it all worthwhile.

What's been the most challenging thing?
Lately, the most challenging and disheartening part has been the rise of misinformation and growing distrust in science and medicine. It's difficult seeing how confusion and fear can stand in the way of prevention, early detection, and lifesaving care—but it has also become one of my strongest motivations. It reminds me why sharing accurate information, telling my story, and building trust through real, human connection matters so much. If even 1 person feels more informed, more confident, or more empowered to act because of that, then the effort is worth it.

What's something that research too often overlooks or gets wrong about what's important to patients?
In research, there is often a strong focus on data points, outcomes, and statistics, but the patient's role and lived experience can be overlooked. Behind every data point is a person navigating their own reality. No 2 journeys are the same, and those differences matter. They shape how patients experience care, make decisions, and move through treatment and survivorship. When we take the time to listen, we gain a fuller understanding that data alone cannot provide.

HEOR often involves assessing costs vs benefits of treatments. In your opinion, what is one type of cost and one type of benefit that aren't considered often enough in these analyses?
One type of cost that isn't considered often enough is the emotional and psychological toll on patients and their families, specifically the anxiety, uncertainty, and disruption to identity and daily life that comes with a diagnosis and treatment. These aren't easily quantified, but they are very real and can shape outcomes in profound ways. Patients are not just participants in a study, they are partners in it, and their voices deserve to be heard, valued, and reflected in the work we do.

On the other side, one benefit that deserves more attention is the value of hope and empowerment that comes from access to information, preventive care, and early intervention. When patients feel informed, heard, and supported, it can influence not only their health decisions but also their quality of life and long-term outlook.

Joslyn Chaiprasert-Paguio is a cancer survivor, Cervivor podcast host and ambassador, patient advocate for cervical cancer and human papillomavirus awareness, and Senior Journal Publisher at Elsevier. She is based in Southern California.

FROM THE PATIENT

"When Patients Are Not Included, Studies Can Be Technically Strong but Miss What Matters."

David Kelly
Operations Manager, Global Heart Hub

How did you become involved in advocating for and/or participating in patient-centric outcomes research?
I was born with a congenital heart defect that was picked up by a routine stethoscope check at age 4, and I underwent a valvotomy just weeks later. When I underwent further open-heart surgery at age 46, I was initially given a choice of 2 valve types. Through my own research I found a third option and a surgeon in Ireland who could perform it. After what I consider a textbook shared decision-making process, I ended up having the surgery that I felt best suited my life and needs—the one that was not initially put forward as an option.

Through that patient journey, I became aware of Global Heart Hub (GHH), and I was delighted to join its team as Ops Manager in 2022. Noting a lack of high-quality, patient-led research about the experience of being diagnosed and living with high cholesterol, GHH made its first significant move into patient-led and patient-centric research with a project documenting patient experiences in 3 countries with very different health systems: Australia, Brazil, and the United States. The findings were presented at 8 major medical congresses, including ISPOR 2024. In fact, that study was so successful that we are now engaged in a similar project focused specifically on the experiences of women with cardiovascular disease.

What's been the most rewarding thing for you about being a patient expert?
There are several:
- Helping patients and caregivers feel like someone gets what they're going through
- Helping to address barriers and bridge gaps between doctors and patients when it comes to their cardiac care
- The work we do to improve system-delivered care
- Building global connections

What's been the most challenging thing?
Some that I personally struggle with at times:
- Navigating medical complexity, especially things like what puts you at risk, interconnected conditions, and the latest treatments.
- Patients not being taken seriously by medical professionals or researchers. This is why involvement in patient-led research is crucial, as it gives patients a more comprehensive understanding of their experiences.
- Feeling pressure to represent diverse experiences. Every patient's experience is unique and can't be taken as a representation of an entire community.
- Balancing patient expert responsibilities with other parts of life like work, family, and paying for healthcare.

What's something that research too often overlooks or gets wrong about what's important to patients?
Gaps include:
- Overemphasis on clinical outcomes. "Quality of life" factors can be treated as secondary when for many patients they are a primary consideration. Likewise, adherence is often framed as a patient problem rather than a system design issue.
- Ignoring emotional and social impacts. Research doesn't always capture the fear of recurrence, its impact on relationships, or depression and isolation after a diagnosis.
- Lack of diversity in patient voices. Many studies still underrepresent women, older adults with multiple conditions, ethnic minorities, or lower-income groups.
- Focusing on single diseases when patients often live with many. Siloed research misses how treatments interact or compete in real life. GHH is part of a growing movement to discourage those models.
- Not involving patients early enough. When patients are not included in shaping research questions, study design, and outcome measures, studies can be technically strong but miss what actually matters.

HEOR often involves assessing costs vs benefits of treatments. In your opinion, what is one type of cost and one type of benefit that aren't considered often enough in these analyses?
An underconsidered cost is patient and caregiver time. For patients, especially those with chronic illness, time is a scarce and meaningful resource. Lost work hours, reduced personal time, and caregiver burden can significantly affect quality of life, yet are often excluded or only roughly estimated in models.

An underconsidered benefit is improved daily functioning and independence in everyday activities like working and socializing. Existing tools for measuring health-related quality of life may not fully capture the nuanced improvements that matter most to individuals.

David Kelly is the Operations Manager for Global Heart Hub, the first global nonprofit established as a voice for patients living with cardiovascular disease. He is based in Galway, Ireland.

FROM THE PATIENT

"Sometimes Patient Voices Are Invited to the Table but Not Fully Integrated Into Decisions."

Kevin Wake
Independent Patient & Sickle Cell Advocate

How did you become involved in advocating for and/or participating in patient-centric outcomes research?
My involvement in advocacy began after my career in pharmaceuticals ended due to health complications from my sickle cell disease. My passion grew from simply assisting other patients navigating a similar journey to using my lived experiences to narrow gaps in patient care, reduce barriers, and review what healthcare systems measure.

As I became more engaged in advocacy, I realized that patients bring critical insights into what truly matters in care—quality of life, pain management, and daily functioning. This led me to participate in research discussions, advisory groups, and outcomes initiatives that elevate the patient voice. I believe patients should not only be subjects of research, but active partners in shaping the questions, outcomes that matter most to them, and solutions that improve care for our communities.

What's been the most rewarding thing for you about being a patient expert?
The most rewarding part of being a patient expert is knowing that my lived experience can help shape better care for others. By sharing my perspective, I can help researchers and healthcare leaders understand what truly matters to patients beyond clinical data. It's powerful to see patient voices influence research questions, care models, and policies that impact real lives.

I also value helping other patients feel heard and empowered. When patients are recognized as partners in research and decision making, it leads to more meaningful outcomes and more compassionate healthcare systems.

What's been the most challenging thing?
One of the most challenging parts is ensuring that patient perspectives are not just heard, but truly valued and acted upon. Sometimes patient voices are invited to the table but not fully integrated into decisions. Often, patient voices are sought only to "check a box" that patients were involved.

Navigating technical research language and complex healthcare systems also can be hard. Despite these obstacles, I continue to speak up, because more patient involvement will lead to better research, more relevant outcomes, greater trust from patients, and ultimately better care for the communities we serve.

What's something that research too often overlooks or gets wrong about what's important to patients?
Research often focuses on clinical measures and numbers while overlooking what patients experience in daily life. Things like pain burden, fatigue, mental health, the ability to work, maintain relationships, or simply get through a normal day are sometimes not captured in traditional outcomes. Patients care deeply about quality of life, not just lab results or hospitalizations.

Another challenge is that researchers may assume what matters to patients without asking them directly. When patients are meaningfully involved from the start, research becomes more relevant and better reflects the real challenges people face when living with chronic conditions.

HEOR often involves assessing costs vs benefits of treatments. In your opinion, what is one type of cost and one type of benefit that aren't considered often enough in these analyses?
One cost that is often overlooked in HEOR is the emotional and psychological burden of living with a chronic condition. Stress, trauma, and the impact of repeated healthcare experiences affect engagement, adherence, and overall well-being but are rarely quantified.

One benefit that is not considered enough is improved quality of life and the benefit long-term. The ability to work, attend school, maintain relationships, and live independently are meaningful benefits beyond clinical outcomes. These real-life improvements are imperative in evaluating the true value of treatments.

Kevin Wake is the former President of the Uriel E. Owens Sickle Cell Disease Association of the Midwest, a Board member for the International Consortium for Health Outcomes Measurement, and an independent patient and sickle cell advocate based in Kansas City, Missouri.

FROM THE PATIENT

"Our Focus Is Ensuring Evidence Reflects Real Patient Priorities and Informs Better Decisions."

Angie Botto-van Bemden
Patient Partner, Musculoskeletal Research International

How did you become involved in advocating for and/or participating in patient-centric outcomes research?
My involvement grew from working across research and development, medical affairs, and patient advocacy, where I saw a persistent gap between what was measured and what truly mattered to patients. We were already codesigning care and running pragmatic trials around real preferences before "patient centricity" became a buzzword. EUPATI (the European Patients Academy on Therapeutic Innovation) validated that high-quality patient involvement/engagement isn't optional—it is essential for credible, fit-for-purpose evidence. Without quality public and patient involvement (PPI)/engagement, HEOR risks measuring what is easy instead of what is meaningful. Our focus is ensuring that evidence actually reflects real patient priorities and informs better decisions.

What's been the most rewarding thing for you about being a patient expert?
Changing the narrative from passive participation to active, informed partnership. Patients are increasingly confident and equipped to define what matters, participate in decisions, and influence development earlier. When patients are partners, research becomes more efficient and impactful. For example, in sarcopenia, patients prioritize function (eg, transferring groceries from cart to car) over muscle mass—functional independence over biomarkers or clinical endpoints. Realizing that patient insights redirect resources toward meaningful outcomes is so rewarding! The biggest reward is knowing that authentic patient engagement in HEOR and improved health literacy lead to better evidence and better health for all.

What's been the most challenging thing?
The gap between rhetoric and reality. Patient centricity is so often stated but not actually operationalized. Research is still designed without patients, plain language is a courtesy or inconsistent, and engagement can be performative rather than a collaborative partnership. Health literacy remains a huge global barrier, and digital advances risk increasing inequities if not intentionally addressed. Meaningful patient partnership requires cogovernance, accountability, and investment. Closing this gap is complex, yet necessary to ensure patients can access and act on the right care or research opportunities at the right time. We hope readers will reach out and partner with patients (via ISPOR's Patient-Centered Special Interest Group) so we can!

What's something that research too often overlooks or gets wrong about what's important to patients?
It too often prioritizes convenience and clinical proxies over lived experience. It misses daily realities: fatigue, fear of the unknown/expected, loss of independence/cognitive autonomy, caregiver exhaustion/strain/impact beyond clinical proxies, future/life/family planning, participation, productivity, hope, family spillover, etc. Patients prioritize function over biomarkers/endpoints; for example, demonstrating a 20% increase in muscle mass doesn't suffice if the improvement is not enough for the patient to help pick up a family member after a fall. This means evidence must be understandable to deliver value, and measures must be meaningful to make a difference. Health literacy and quality PPI are non-negotiable for relevant HEOR. Evidence without patient partnership may be rigorous, but it's irrelevant.

HEOR often involves assessing costs vs benefits of treatments. In your opinion, what is one type of cost and one type of benefit that aren't considered often enough in these analyses?
A cost that isn't considered enough is the cumulative patient/caregiver burden: lost income, time, coordination, and cognitive/emotional strain are invisible in claims data and traditional analyses.

A benefit that isn't considered enough is restored agency—the ability to work, plan, participate, and live with hope or less fear. Whole-health frameworks are important, yet undervalued. HEOR *must* evolve to capture whole-person value. Prompting early patient involvement, prioritizing health literacy, and applying broader value frameworks are critical to ensuring that analyses reflect what truly matters.

Angie Botto-van Bemden is Executive Director and Founder of Musculoskeletal Research International and Chair of ISPOR's Patient-Centered Special Interest Group. She is based in Tampa, Florida.

By the Numbers: Patient Centricity in Healthcare

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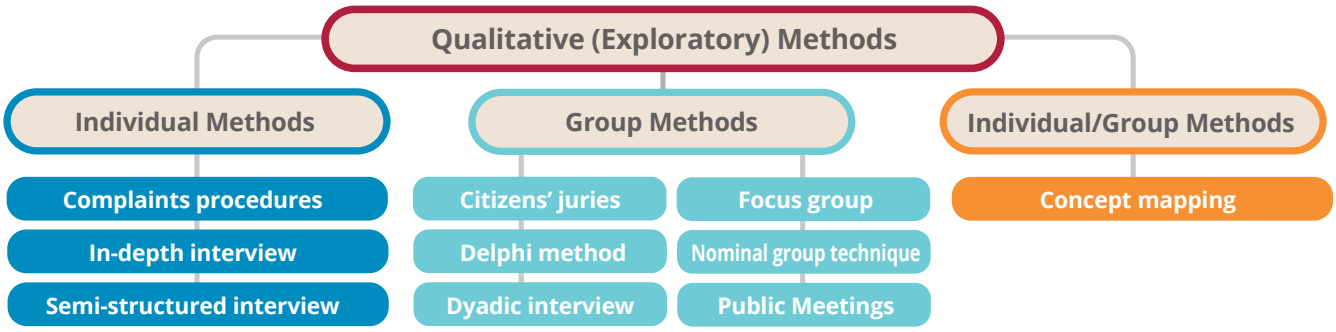
Patient Preference Exploration Methods



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How Health Systems Are Moving Patient Engagement Beyond Token Participation

PATIENT ENGAGEMENT IN HEALTHCARE DECISION MAKING

Drug Development/ Regulatory Review

FDA Patient-Focused Drug Development meetings (United States)

EMA advisory committee meetings (Europe)

Impact

25+ disease areas studies through PFDD meetings

700+ EMEA stakeholder interactions

Reimbursement Decisions

NICE (United Kingdom)
Canada's Drug Agency (Canada)
G-BA (Germany)
HAS (France)

Impact

Incorporated across HTA programs

Formal integration into coverage deliberations

Clinical Care Delivery

Family-centered rounds

Impact

37.9% fewer errors across 3106 admissions in 7 hospitals

EMA indicates European Medicines Agency; FDA, US Food and Drug Administration; G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de santé; NICE, National Institute for Health and Care Excellence.

Beyond Tokenism: Meaningful Patient Engagement

The 3 domains to address when evaluating and improving patient engagement

METHODS & STRUCTURE | INTENT | RELATIONSHIP BUILDING

5 Key Strategies:

1. **Start with genuine intent** Patient Experience must actively shape research—not merely validate it.
2. **Engage longitudinally** Involve patients throughout the full research lifecycle, not just at milestones.
3. **Address power imbalances** Uneven dynamics are the most common barrier—name and actively counter name.
4. **Build patient capacity** Provide training and mentorship so patient partners can contribute fully.
5. **Recruit for diversity** Measure and report the diversity if patient partners. Representative recruitment is both an ethical imperative and a quality indicator for genuine engagement.

RESEARCH ROUNDUP

Section Editor: **Aakash Bipin Gandhi, BPharm, PhD**, Sanofi, Cambridge, MA, USA

An access-focused patient-centric value assessment framework for medication formulary decision-making in immune-mediated inflammatory diseases.

Yang M, Mittal M, Fendrick AM, et al. 2025. *Adv Ther*. 2025;42(2):568-578.

Summary

The authors propose an access-focused patient-centric value assessment framework for formulary decision making in immune-mediated inflammatory diseases. They argue that traditional approaches are inadequate given the evolving immune-mediated inflammatory disease treatment landscape, where medications are approved for multiple indications and treatment targets have advanced beyond clinical trial endpoints. The access-focused patient-centric framework encompasses 3 core value components: (1) achieving therapeutic goals, (2) improving health-related quality of life, and (3) enhancing work productivity with monetization derived from clinical trial data when real-world evidence is unavailable. Patients and their families are positioned at the top of the healthcare ecosystem pyramid, supported by utilization management protocols guided by policy makers, payers, and employers.

Relevance

This article contributes to the broader discussion of patient-centric value assessment by proposing a structured framework that explicitly incorporates patient-relevant outcomes beyond traditional clinical endpoints. The framework's focus on quality of life and work productivity reflects growing recognition that value in healthcare must encompass dimensions that matter to patients themselves. By attempting to monetize these patient-centered outcomes, the authors provide a practical approach for translating patient priorities into the formulary decision-making processes.

Insights for resilient and patient-centric healthcare systems.

Sparacino L, Schmid A. 2026. In: *Organizational Insights: Healthcare Perspective: An Introduction to the Dynamics of Healthcare Excellence*. Cham: Springer Nature Switzerland; 2026:49-68.

Summary

The authors examine how technology, particularly telehealth and decentralized healthcare delivery, can create more resilient and patient-centric systems. They emphasize that patient preferences vary greatly based on individual circumstances, life stages, and cultural contexts, and advocate for an "ethics of care" approach to policy making that considers the relational and contextual nature of healthcare decisions. Authentic community engagement is stressed as essential, with explicit warnings against tokenistic consultation. The authors recommend 3 principles: fostering cocreation within and across communities, promoting coordination of simple and integrated health systems, and creating agile systems that accommodate variable patient and community needs.

Relevance

This article offers clear articulation of what genuine patient centricity looks like in practice, moving well beyond token participation by advocating for authentic cocreation with communities. The authors' warning against tokenistic engagement directly addresses the core concern of this issue, although it also reveals the complexity of balancing individual preferences with population health needs and navigating power dynamics between institutions and diverse communities.

How to fix a broken healthcare system: pathways to maximize health and well-being for all.

Chin MH, Bruch JD, Grogan CM, et al. *Diabetes Care*. 2026;49(1):44-62.

Summary

The authors present a comprehensive analysis of US healthcare system failures—using diabetes care as a model for systemic problems—and argue that the fundamental issue is the system's failure to prioritize the long-term health and well-being of all individuals and communities. Three foundational elements are identified: ethics and culture, political economy, and the definition and measurement of value in healthcare. Policy recommendations include anchoring healthcare in ethics and justice, implementing principles of good governance, measuring social return on investment, reforming health insurance toward universal coverage, and addressing social determinants of health. The authors stress that sustainable reform requires both technical policy changes and fundamental cultural shifts toward valuing the health of all Americans, particularly marginalized populations.

Relevance

This article provides a comprehensive framework for understanding systemic barriers to patient centricity, demonstrating that the current system's prioritization of short-term financial gain is precisely why patient perspectives remain marginalized in value assessments. The authors' call for fundamental shifts in ethics, political economy, and value measurement suggests that healthcare systems are not ready for genuine patient centricity without major structural transformation, making incremental improvements in patient engagement insufficient on their own.

Note from the Section Editor: *Views, thoughts, and opinions expressed in this section are my own and not those of any organization, committee, group, or individual that I am affiliated with.*

Bridging Theory and Practice to Advance Patient-Centered Economic Evaluation of Health Technologies

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KEY TAKEAWAYS

Patient-centered economic evaluation incorporates patient engagement and high-quality patient experience data throughout the economic evaluation component of health technology assessment.

This comprehensive approach enhances the scientific rigor of economic models and supports decision making that is aligned with patient needs and priorities.

Health technology assessment bodies, researchers, and patient groups should collaborate to raise awareness, clarify expectations, and scale adoption of patient-centered economic evaluation.

Economic evaluation is often a critical component of the health technology assessment (HTA) process. It attempts to provide a comprehensive analysis of the economic ramifications associated with integration of new health technologies into healthcare systems and inform reimbursement and pricing decision making. The goal is to allocate scarce resources to interventions that provide the most overall value to patients, healthcare systems, and society.

Patients are experts in living with their diseases and can offer valuable insights into the real-world impact of disease and health technologies. Integrating patient experiences into economic assessments can lead to decisions that more closely align with patient needs and values, thereby optimizing healthcare decision making and resource allocation.

This article will discuss the importance of patient-centered economic evaluation, how it is conducted, real-world examples, and courses of action to inspire broader adoption.

What Is Patient-Centered Economic Evaluation?

Defining a few key terms will provide a foundation for this discussion. ***Patient engagement*** in research is defined as "active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process."[1] ***Patient experience data*** (PED) are "intended to provide information about patients' experiences with a disease or condition," including "the impact of such disease or condition, or a related therapy, on patients' lives… [and] patient preferences with respect to treatment of such disease or condition."[2] ***Patient-centered economic evaluation*** is conducted through the engagement of patients as research partners and the application of high-quality PED throughout HTA processes.

Patient-centered economic evaluation in HTA is often mistakenly viewed as incorporating patient out-of-pocket costs as inputs and/or estimating quality-adjusted life years as outputs. This view primarily reflects the perspectives of HTA bodies and researchers, and may not capture outcomes, values, and costs that matter to patients. The inclusion of those outcomes, values, and costs determines whether an evaluation is patient centered.

Why Is It Important?

Patient-centered economic evaluation plays a crucial role in enhancing the scientific rigor of the economic model. Patient research partners and PED can provide valuable insights for establishing realistic assumptions grounded in actual patient experiences, creating a valid model structure that more accurately reflects disease progression and its impact, selecting the best available model inputs, and utilizing outcome measures that capture what is important to patients. Patient research partners can also help identify limitations within the economic model and highlight areas where the model may not adequately reflect their experiences or the complexities of their conditions and daily lives; this is essential for identifying potential biases and gaps in the model for decision makers' consideration.

> Patients are experts in living with their diseases and can offer valuable insights into the real-world impact of disease and health technologies

Incorporating the experiences and preferences of patients into the economic evaluation process ensures the evaluations better reflect the actual needs and priorities of patients, while fostering greater transparency and trust in the decision-making process. Ultimately, this alignment can result in more effective allocation of resources, improved health

outcomes, and enhanced patient satisfaction within the healthcare system.

How to Conduct Patient-Centered Economic Evaluation

Recommendations from patient-centered research organizations and HTA bodies can guide the conduct of patient-centered economic evaluations. The Patient-Centered Outcomes Research Institute's Foundational Expectations for Partnerships in Research,[3] the Patient Focused Medicines Development's Patient Engagement Quality Criteria,[4] and the National Health Council's (NHC) Rubric to Capture the Patient Voice[5] provide fundamental principles for meaningful, effective, and sustainable patient engagement. Health Technology Assessment International and HTA bodies such as the National Institute for Health and Care Excellence and the Institute for Clinical and Economic Review have established high-level guidelines for patient engagement that may also be informative to patient-centered economic evaluations.[6-8]

> Together, engagement of patients as research partners and high-quality patient experience data provide comprehensive insights that ensure economic evaluations are patient-centered.

The NHC's Patient-Centered Value Model Rubric was developed to guide researchers in incorporating patient engagement into economic evaluations. It lists characteristics of meaningful patient engagement and considerations to enhance the patient-centeredness of economic evaluations with examples across 6 domains: patient partnership, transparency to patients, inclusiveness of patients, diversity of patients/populations, outcomes patients care about, and patient-centered data sources.[9]

Additionally, frameworks for engaging patients in other types of research have been leveraged by researchers to guide patient-centered economic evaluations. These include the 10-Step Framework for Continuous Patient Engagement in Comparative Effectiveness Research,[10] the Conceptual Modeling Framework for Public Health Economic Modeling,[11] and the Framework for Public Involvement in Mathematical and Economic Modelling.[12]

Beyond effective patient engagement, researchers should proactively seek high-quality PED to inform their work. PED encompasses patient experiences collected through a broad range of qualitative, quantitative, or mixed research methods. To be of value to multiple stakeholders, high-quality PED should be patient-engaged, meaningful, representative of diverse patient populations, and fit-for-purpose.[13] Researchers must evaluate if published or newly collected PED accurately captures patient experiences, considering its patient-centricity, validity, and reliability, and transparently noting any limitations, such as lack of sample representativeness and associated constraints on generalizability, or potential bias introduced by missing data and nonresponse.[14,15]

Engagement of patients as research partners and high-quality PED are complementary: Engagement yields insights PED may miss, while PED can encompass broader patient populations. Together, they provide comprehensive insights that ensure evaluations are patient centered.[16]

Real-World Examples and Lessons Learned

We did not identify any publications on PED in economic evaluations as a component of HTA. Patient engagement remains uncommon in economic evaluations, although we identified 4 papers that describe engagement processes and their effects (**Table**, next page).

- Mattingly et al[17] assessed the cost-effectiveness of drug therapy for hepatitis C virus when considering non-health costs, such as patient/caregiver time and productivity, in addition to sustained virologic response.
- Al-Janabi et al[18] worked with current or recent family caregivers to develop research methods for measuring and valuing the quality of life of family carers.
- Wilson et al[19,20] engaged patients and caregivers in assessing the costs and benefits associated with chimeric antigen receptor T-cell (CAR-T) therapy for adults with acute lymphoblastic leukemia.
- Bunka et al[21] included patient partners in the design and development of an economic simulation model of care pathways for major depressive disorder.

Patient engagement was operationalized using various methods, from consulting with individual patients[19-21] to having a Lived Experience Advisory Panel of caregivers[18] or a Stakeholder Advisory Board that included patients with other stakeholders.[17] Advisory committees represent a widely recognized and effective method of stakeholder engagement. We recommend that researchers utilize a framework such as the NHC's Rubric to Capture the Patient Voice[5] to inform the governance and policies of these committees. We also recommend multiple patient partners representing diverse disease experiences. However, when resources such as funding, time, or personnel are limited, engaging 1 or 2 individual patient partners can be beneficial, although not optimal. Regardless of resource availability, researchers should have a solid understanding of the disease and patient life experiences by reviewing PED literature, in addition to consulting with patient partners.

These studies provided a limited description of patient engagement processes. Patient partner recruitment was reported solely by Al-Janabi et al.[18] Engagement formats were briefly described as meetings and/or emails,[17-21] with Bunka et al noting that the precirculation of documents before meetings facilitated preparation.[21] This lack of detail restricts our ability to fully assess the quality, variability, and effectiveness of engagement approaches and highlights the need for more comprehensive documentation and transparency.

Patient partners contributed to the studies by actively engaging in setting research questions, refining study designs, improving data collection and analysis, highlighting study limitations,

Table. Patient Engagement and Impact Reported in Economic and Disease Modeling Publications

Study	Mattingly et al[17]	Al-Janabi et al[18]	Wilson et al[19,20]	Bunka et al[21]
Study Focus	HCV treatment CEA	Incorporating caregiver QoL into economic evaluation	Early CEA of CAR T-cell therapy for R/R B-cell ALL	Major depressive disorder care pathway model
Patient Partner	11-member SAB including 4 HCV patients and 1 patient advocate	A LEAP made up of 5 people with current or recent diverse family caregiving experience	1 patient partner + 2 group discussions involving patients and caregiver	2 patients
Recruitment	NR	Through mental health charity organizations and a colleague	NR	NR
Engagement Format	11 SAB meetings held over 3 years across project stages	The LEAP and researchers met 12 times over 4 years	Through multiple project meetings and regular email correspondence	Through meetings, documents were pre-circulated to facilitate preparation
Patient Partner Role	• Reviewed model's structure, inputs, outcomes, and results presentation • Provided iterative input and qualitative discussion • Informed methods of Delphi process and economic model	Gave input on: • Focus group recruitment and interview • Transcript coding • Questionnaire and Delphi study design • Think-aloud interview • PTO design and dissemination	Gave input on: • Research questions • Study design • Recruitment strategy/ consent process/plan for analysis	• Enhanced the model's language • Improved flow diagrams • Challenged assumptions • Validated treatment pathways • Highlighted limitations • Generated new research questions
Impact	• Identified fear of harming others as a key issue for HCV. • Identified indirect costs that led to development of ILYs and workdays missed as health outcomes.	• Created new recruitment and dissemination channels • Enhanced survey accessibility • Ensured open and honest responses	• Improved recruitment efforts • Enhanced discussions with patients and caregivers • Ensured reflective and representative analysis	Resulted in a more accurate model that reflects current standards of care
Learnings	NR	• Researchers and lay participants need training and preparation • Practical measures and soft skills are needed for ongoing engagement • Care needed when selecting research tasks for PPI	• More time was needed to ensure the patient partner's comfort in engaging • Attention was necessary to avoid an undue power dynamic between the patient partner and research participants	• Meaningfully include patient partners for model enhancement and validation • Embrace uncertainty as a team • Share experiences authentically, incorporating patient perspectives for broader learning

CAR T-cell therapy indicates chimeric antigen receptor T-cell therapy; CEA, cost-effectiveness analysis; HCV, hepatitis C virus; ILYs, infected life-years; LEAP, lived experience advisory panel; NR, not reported; PPI, patient and public involvement; PTO, person trade-off; QoL, quality of life; R/R B-cell ALL, relapsed or refractory B-cell acute lymphoblastic leukemia; SAB, stakeholder advisory board.

creating new avenues for dissemination, and generating new research questions that could guide future investigations. Their contributions led to identification of important health outcomes, improved recruitment efforts, enhanced communication with patients and caregivers, facilitated a reflective and representative analysis, and resulted in more accurate models.[17-21]

Among the key engagement learnings from the studies, authors noted that effective collaborations require time and preparation, alongside practical measures and soft skills to ensure ongoing engagement.[18-20] Wilson et al highlighted the potential for a power imbalance between the patient partner and patient research subjects, despite the fact that patient and public involvement helped equalize power between the academic team and the patient and caregiver participants.[19,20] This underscores the importance of actively managing roles and expectations so that patient partners are empowered without inadvertently exerting influence over other patients' contributions. We also emphasize the importance of recognizing and addressing power

imbalances between researchers and patient partners as an important consideration in patient-centered research more generally.[22,23]

Al-Janabi et al suggested that researchers assign specific tasks for patient engagement.[18] However, we contend that this approach can limit the scope of engagement and imply that patients are only capable of limited roles. Instead, patients should be engaged as equal research partners across all stages, fostering a genuinely collaborative environment. This can be operationalized by co-creating roles and responsibilities with patient partners, allowing flexibility and ongoing negotiation of contributions.

Discussion

As rising healthcare costs globally place unsustainable pressure on healthcare systems, many patient needs remain unmet. Patient-centered economic evaluation incorporates patient experiences to help ensure that healthcare resources are allocated to interventions addressing the most pressing needs of patients.

Despite examples of successful collaboration between researchers and patients, patient-centered economic evaluation in the context of HTA has not yet become commonplace. Few HTA guidelines require the incorporation of patient engagement and PED throughout the economic evaluation process. Guidelines' emphasis on uniform inputs and standardized methods limits opportunities for meaningful patient engagement. In addition, researchers may underestimate the value of patient-centered economic evaluation and lack incentives to adopt this approach. Addressing these multifaceted barriers through multistakeholder approaches is essential to advancing patient-centered economic evaluation.

HTA bodies should collaborate with researchers and patients/patient groups to establish guidelines and standardized methods recommending that patient experiences be systematically considered in economic evaluations. They should also ensure that their decision-making processes prioritize economic evaluations that better reflect patient perspectives. Researchers should receive targeted training to develop the skills needed for effectively engaging patients, including the ability to communicate complex concepts in plain language and gather meaningful patient input, supported by mentorship from patient engagement experts. Patients/patient groups should actively advocate for their inclusion in the economic evaluation process so that their lived experiences can inform more impactful research and healthcare decisions.

By fostering collaboration among HTA bodies, researchers, and patients/patient groups, the healthcare system can create a more inclusive environment for economic evaluations that are not only rigorous but also relevant and beneficial to the patients being served.

Disclosures: Nan Qiao is an employee of MSD. This work was written in her personal capacity, outside of her employment, and is unrelated to her role at MSD.

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Industry Stakeholders Reflect on Patient Centricity's Progress and Prospects for a More Equitable Future

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KEY TAKEAWAYS

The biopharmaceutical industry is increasingly focusing on patient priorities and needs in managing diseases. However, it is challenging to achieve true patient centricity within clinical trials and regulatory frameworks.

Collecting patient experience data, including patient-reported outcomes, is crucial for understanding heterogeneous patient experiences and informing regulatory decisions.

Without clear return on investment metrics, patient centricity risks becoming a checkbox exercise. To embed it meaningfully, companies need models that track impact.

Biopharmaceutical medicines development has long been focused on scientific innovation. This is essential and has led to the eradication of many diseases as well as significant improvements in the day-to-day clinical management of chronic diseases. However, medicines only work in people who choose to take them,[1] and the desire and drive to answer questions like "What can be done?" in medicines development sometimes led to avoidance of answering questions like "What should be done?".

> Survey data suggest one reason for lack of trust in the biopharmaceuticals industry is the belief that companies are driven by profits rather than the needs of patients.

As a health psychologist, I think about "what should be done" in 2 ways: What is the burden of disease for patients and healthcare systems, and what are the patient and clinician priorities, preferences, and needs in managing that disease? Inclusion of the patient is essential.

Patient Centricity in Medicines Development

Calls for a more patient-focused approach to medicines development have been growing from governments, insurers, and patient organizations for years, and the biopharmaceutical industry is embracing them through the "patient centricity" movement. Companies are now working more closely with patient advocacy groups, and company mission statements have been reworked to reflect a commitment to improving lives.[2]

However, in 2020, a survey of more than 1000 patients from the United Kingdom and Ireland showed that the biopharmaceutical industry is one of the least trusted industries.[3] One reason was because survey respondents believed the approach and priorities of pharmaceutical companies were driven by profits rather than the needs of patients—that companies were not truly committed to the principles of patient centricity but instead were skirting around the idea by starting a few highly visible initiatives without weaving it into the fabric of the organization.

Further reflection and discussion are, therefore, needed.

Collecting Industry Perspectives on Patient Centricity

In early 2025, I asked more than 30 people who work in and around the biopharmaceutical industry for their thoughts on patient-centric intervention development. Specifically, I invited pharmaceutical company executives, small biotechnology manufacturers, patient representatives/patient advocates with lived experiences, patient experience data (PED) researchers, regulatory representatives, and payer and health technology agency (HTA) advisors to reflect on where we are today as an industry, what improvements are still to be made, and whether patient centricity offers a genuine shift for the future of healthcare. They could offer their thoughts through a personal narrative, a review of the research, a poem, a series of drawings, or whatever made sense to them.

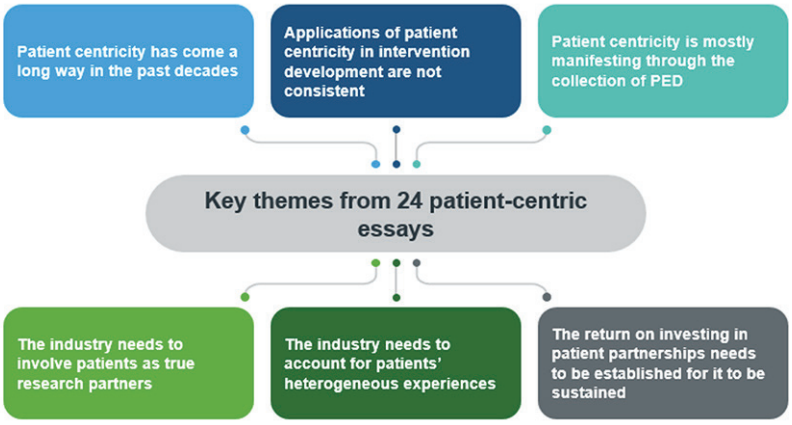
The contributions were collated and bound in a book in April 2025.[4] Only stylistic editing has been applied to their musings and the views presented are therefore somewhat unfiltered and honest, grounded in the authors' own experiences, knowledge of and/or participation in research, and hopes for the future.

See **Figure 1** for a list of contributor organizations.

Figure 1. Contributor organizations

- US Food & Drug Administration (FDA)
- Heartbeat
- University of Tasmania Menzies Institute for Medical Research
- Ferring Pharmaceuticals
- Accelerated Cure Project for Multiple Sclerosis (MS)
- Astellas
- Prostate Cancer Research
- Boehringer Ingelheim
- Paladin Consortium
- Imbria Pharmaceuticals
- Gibson Research Ltd.
- Angela Radcliffe
- IQVIA Patient Centered Solutions (PCS)
- Tufts Center for the Study of Drug Development (CSDD)
- Novartis
- LUNGevity
- Sanofi
- AbbVie
- CSL Behring
- MediPaCe
- University of Birmingham Centre for Patient Reported Outcomes Research (PCOR)
- Association of the British Pharmaceutical Industry (ABPI)
- Aspen Consulting
- Parkinson's Europe
- Miller Economics Ltd

Figure 2. Key themes across the contributions



A summary of findings from across the contributions was presented at the ISPOR Europe Congress 2025, where the topic was "powering value and access through patient-centered collaboration."[5] This summary is also presented below.

Findings From the Collection

Six clear themes have emerged from the contributions to the collection (see **Figure 2**).

1. We've Come a Long Way.

Not long ago, medicines development rarely involved patients. Products were designed around scientific innovation and researcher convenience, with little regard for patient priorities or experiences. Clinical trials often excluded patient input, and outcomes focused on clinical metrics such as disease progression or biomarkers rather than symptomatic improvement such as reduction in pain or cough, and quality of life.

Thankfully, this has changed. Advances in technology, shifting societal attitudes, and growing patient advocacy have pushed the industry to recognize that successful treatments must be acceptable to both clinicians and patients, in the same way as any consumer product must be acceptable (if not desirable) to the end user or purchaser. Today, it is an expectation—at least in the United States and Europe—and many companies actively seek patient input to ensure new interventions meet real needs. This is particularly true for rare diseases, where heterogeneity in patient experience must be understood to design trials that patients are able to participate in and with measure outcomes that they care about.

2. Patient Centricity Is Still Inconsistently Applied.

While patient-centered medicines development is now expected in the United States and Europe, its application varies widely. Contributors to this collection offered definitions ranging from "listening to patients" to "designing meaningful and accessible interventions." Despite this shared intent, the practical implementation remains inconsistent. True patient centricity is difficult to achieve, especially within the rigid frameworks of clinical trials and regulatory requirements. Too often, patient involvement is limited to short-term consultations that feel more like box-ticking than genuine collaboration. This superficial engagement risks undermining trust in an industry that claims to prioritize patients.

3. Patient Experience Data Is the Main Avenue.

The most common way patient centricity is expressed today is through the collection of PED in clinical trials. PED includes insights into how patients feel, function, and experience their condition and its treatment. The most widely used form of PED is patient-reported outcomes (PROs), which measure symptoms, quality of life, and treatment tolerability from the patient's perspective. These data can inform regulatory decisions, support product labeling, and guide clinical care. However, PROs offer only part of the picture. To truly understand patient experiences, researchers must combine qualitative and quantitative methods—and listen deeply to what matters most to individuals.

4. The Biopharmaceutical Industry Needs to Involve Patients as True Research Partners.

Patient centricity encourages companies to place patients at the center of drug development—but patients don't want to be the sole decision makers. They want to be equal partners alongside clinicians, regulators, and payers. Most patients seek a meaningful voice in shaping interventions, recognizing that their priorities may not always align with clinical or regulatory constraints.

> True patient centricity is difficult to achieve, especially within the rigid frameworks of clinical trials and regulatory requirements.

An equitable model where the patient voice is as valued as other stakeholders is emerging as the optimal approach. This partnership should begin early and continue throughout the development process. Technology, including artificial intelligence and online platforms, can help broaden and sustain these collaborations.

Partnerships should start by identifying patient needs and preferences. Patient partners can then provide feedback on potential treatments, help design clinical programs (including which outcomes

to measure to demonstrate value), and shape trials to reduce participant burdens and improve relevance. Their involvement can also support recruitment, training, and interpretation of results. Post trial, patient partners can help communicate findings and contribute to regulatory submissions and educational materials, as well as design real-world data collection approaches such as registries or observational studies.

To make this model work, companies must embed patient involvement as a core value, supported by standardized frameworks and cross-functional objectives. Education and training—for both industry professionals and patients—are essential to foster effective collaboration.

> Most patients seek a meaningful voice in shaping interventions, recognizing that their priorities may not always align with clinical or regulatory constraints.

One novel example of this in a pharmaceutical company involved a Global Head of Patient Centricity overseeing teams focused on integrating the patient perspective in discovery and early development as well as in a real-world setting, in addition to teams focused on culture and integration, partnership, and behavioral science.[6]

5. Patient Partnerships Must Account for Heterogeneous Experiences.
Not all patients have the same experiences, and one voice cannot represent all. Contributors to the collection highlighted the lack of diversity in drug development and called for broader inclusion across race, ethnicity, socioeconomic status, geography, and health literacy. Without this, interventions risk being irrelevant to large segments of the population.

Partnering with patient advocacy groups and charities can help reach underrepresented communities and ensure more inclusive research. While regulators like the US Food and Drug Administration have pushed for diversity in trials in the past, recent political shifts have challenged these efforts. These evolving dynamics have increased the need for companies to continue to prioritize diverse perspectives to ensure treatments serve society as a whole.

6. The Return on Investment in Patient Partnerships Needs to Be Established.
While regulators in the United States and Europe encourage patient-centric development, it's not a global mandate. Contributors agreed it's the right thing to do—ethically and practically—but acknowledge that without clear return on investment (ROI), companies may hesitate to fully commit.

True partnership requires time, resources, and structural changes. The benefits—such as improved product relevance and trust—are real but not always easy to quantify. Some efforts have been made to quantify the ROI of patient engagement for the biopharmaceutical industry, but they have largely been conceptual.

For example, a study by the Clinical Trials Transformation Initiative, in collaboration with Tufts Center for the Study of Drug Development and Janssen, suggested that a modest $100,000 investment in patient engagement may result in savings of up to $2.1 million in avoidance of one substantial protocol amendment in a phase III oncology trial.[7] Other research has suggested that enrollment and retention in clinical trials can be enhanced through PROs.[8] Some progress has also been made in quantifying the ROI for patient engagement beyond clinical trials, like the inclusion of patient-reported outcomes in drug labels and commercialization,[9,10] but findings are not conclusive or particularly persuasive.

Without clear ROI metrics, patient centricity risks becoming a checkbox exercise. To embed it meaningfully, companies need models that track impact from development through approval, reimbursement, and market uptake.

One Year Later

It is now nearly 1 year since the publication of the book that provided these insights from across the industry. In that time, I have attended multiple patient-focused research meetings, engaged with various research collaborations, and been quite vocal about the need for change. In doing so, I have learned that the appetite is there, but that it is not so easy!

> Without clear return on investment metrics, patient centricity risks becoming a checkbox exercise.

Operational and scientific barriers are hard to overcome when designing clinical trials that meet regulatory expectations, and contracting for partnerships between large organizations is wrapped up in complex legal discussions. There is certainly not a lack of interest in patient partnerships.

However, regulations are changing to allow for more long-term strategic involvement of patients through medicines development. For example, the UK revisions to the Clinical Trial Regulations, which come into effect in April 2026, aim to reduce unnecessary burden on participants (including long-overdue simplification of the informed consent process); make trials more flexible, inclusive, and responsive; and increase transparency and trust.[11]

Call to Action

Patient partnership offers a promising path forward. By involving patients throughout the development journey, the industry can create more relevant, effective, and trusted interventions. Now is the time to move from rhetoric to action—and build a future where treatments are truly designed for all of us.

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Unlocking the Voice of Patients: Are Engagement Initiatives Transforming Canadian HTA Reviews?

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KEY TAKEAWAYS

Patient-reported outcome data are key to supporting regulatory and reimbursement decisions that increasingly consider a more holistic perspective rather than strictly focusing on clinical endpoints.

Patient-reported outcome data should be considered starting in early phases of drug development to allow for the most meaningful data to be captured during registrational trials.

The increased emphasis on patients' voices in the development and value of new therapies is being reflected in Canada's Drug Agency reviews, with specific outcome types varying across conditions.

Introduction: The Need for Patient Centricity in Clinical Trials

Traditionally, the evidence supporting drug treatment benefit primarily relied on clinical endpoints, but since the early 1990s, understanding of the importance of incorporating the "patient voice" into the assessment of treatment efficacy and effectiveness has grown. Ultimately, the patient holds the best perspective of their experiences with a particular health state and treatment. While clinical outcome measures provide what are considered "hard," unequivocal outcomes (eg, mortality, lab values, tumor shrinkage), they may not capture factors that impact the patient's quality of life and matter most to the patient. In some cases, the patient experience may differ from treatment effects described by clinical outcomes; to the patient, for example, negative side effects of treatment may outweigh apparent clinical benefits. Thus, the patient experience is critical to understanding and comparing the benefits and risks of treatment.

When treatments have similar primary clinical outcome results (eg, similar survival rates), data from patient-reported outcomes (PROs) can provide information about the impact of treatment on symptoms of the underlying disease, possible side effects, and how those experiences impact a patient's daily activities.[1] Results from PRO data may align with other clinical outcomes (eg, improvement in survival corresponding with improved symptoms), or they may provide contrasting results (eg, improvement in survival but decreased health-related quality of life [HRQoL]). Moreover, some progressive diseases, such as rheumatoid arthritis, lack objective patient-relevant clinical endpoints. Developing and utilizing standardized PRO measures allows healthcare providers and researchers to assess patient symptoms, functioning, and HRQoL in ways that can be compared across groups of patients (eg, in clinical trials) or over time (eg, to assess patient response to treatment).[2]

Over the past 25 years, regulatory bodies such as the US Food and Drug Administration and the European Medicines Agency have become increasingly focused on taking the patient perspective into account when evaluating drug benefits. Similarly, health technology assessment (HTA) agencies have developed their own patient engagement strategies to better understand the value of treatments. Although HTA reviews are conducted separately from regulatory reviews, both are typically based on the same registrational trials, amplifying the impact of decisions made during trial design.

We sought to assess how Canada's Drug Agency (CDA-AMC) has included the patient perspective in its HTA reviews and how increasing emphasis on the patient experience has impacted the data available to inform this evaluation.

How Does CDA-AMC Involve Patients in the Reimbursement Process?

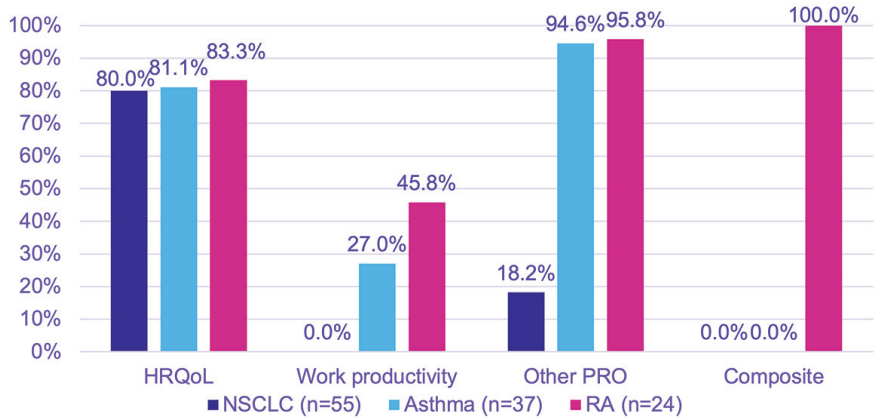
Under CDA-AMC, patient involvement in the reimbursement process has been relatively straightforward (**Figure 1**). Prior to conducting a review, CDA-AMC solicits input from patient groups, summarizes that input, and validates it with the patient groups. Following the review, patient feedback is requested on the recommendations. Patient input generally covers their experience with

Figure 1. CDA-AMC patient involvement

CDA-AMC indicates Canada's Drug Agency.

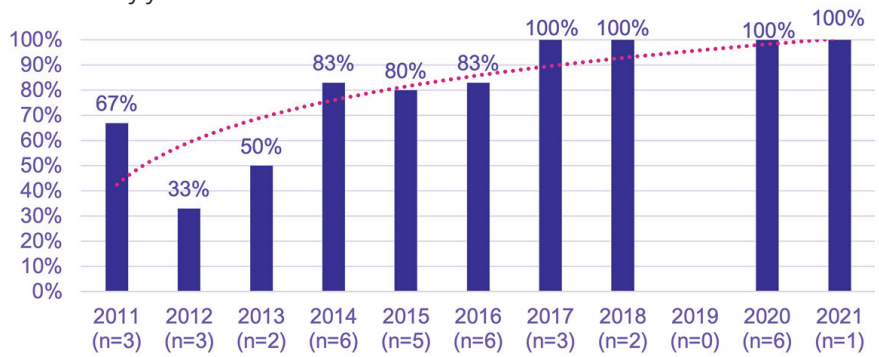
the disease and currently available treatments, unmet needs, and outcomes that are important to patients. In the methodology guidance for HTA reviews, CDA-AMC states that the outcomes of interest should include "clinically meaningful endpoints such as mortality, morbidity, and patient-reported experiences, symptoms, health behaviors, function, and HRQoL."[3] Additionally, in January 2026, CDA-AMC announced its updated patient group input process, including a revised Patient Group Input Template designed to align patient input with the 5 domains of value: clinical value, unmet clinical need, distinct social and ethical considerations, economic considerations, and impacts on health systems.[4]

Figure 2. Types of outcomes reported in trials in CDA-AMC reimbursement reviews



CDA-AMC indicates Canada's Drug Agency; HRQoL, health-related quality of life; NSCLC, non-small cell lung cancer; PRO, patient-reported outcome; RA, rheumatoid arthritis.

Figure 3. Asthma trials in CDA-AMC reimbursement reviews that included HRQoL measures by year



CDA-AMC indicates Canada's Drug Agency; HRQoL, health-related quality of life.

Do Reimbursement Reviews Include the Data That Really Matter to Patients?

In our evaluation of HTAs submitted to CDA-AMC, we focused on drug treatments for 3 conditions: non-small cell lung cancer, asthma, and rheumatoid arthritis. The 3 conditions were chosen because they exemplify the continuum of ways in which the subjective patient experience is incorporated into clinical outcomes.

- The main clinical outcomes used in assessing therapies for rheumatoid arthritis rely heavily on patients' evaluations of their pain, ability to carry out daily activities, and global disease assessment.
- Clinical outcomes for asthma are more objective measures of lung function, but patient-reported symptoms are also commonly included.
- Non-small cell lung cancer clinical outcomes focus on objective measures of survival and response.

Most trials included in the CDA-AMC reimbursement reviews on treatments for non-small cell lung cancer (n=55 trials), asthma (n=37 trials), and rheumatoid arthritis (n=24 trials) reported at least some PRO data, although the types of PROs varied by condition (**Figure 2**).

The PROs captured in these trials have been categorized here as HRQoL, work productivity, composite outcomes (ie, outcomes that include some patient-reported information [such as pain] combined with clinician assessment, global disease assessment, and/or purely objective measures such as lab values), or other PROs (eg, specific disease symptoms, global assessments of disease, satisfaction with treatment). Across the indications, HRQoL was the most common type of PRO assessed; all rheumatoid arthritis trials also included at least one composite outcome (most commonly the American College of Rheumatology response criteria). Nearly all asthma and rheumatoid arthritis trials included at least one other PRO, typically assessing specific symptoms such as pain, fatigue, wheezing, or coughing. Additionally, patient-reported work productivity has been incorporated into some asthma and rheumatoid arthritis trials. Although the number of trials each year was small, the inclusion of HRQoL in asthma trials has increased over time (**Figure 3**).

What Should We Target Next?

The results of our exercise indicate that HRQoL was assessed in the majority of non-small cell lung cancer, asthma, and rheumatoid arthritis trials included in CDA-AMC reviews. The specific PRO measures used across studies varied; some used generic HRQoL scales (eg, EQ-5D), while others used disease-specific scales.

In the 30 asthma trials that assessed HRQoL, most used the Asthma Quality of Life Questionnaire. However, there was variation in the version of the questionnaire that was used. When looking at the tools used to assess symptoms in asthma trials, the landscape is even more heterogeneous. Although there are methods for quantitatively comparing different tools used to assess the same construct, these methods often reduce interpretability

of the data.[5] In addition, some of the methods (eg, using a threshold to convert continuous measures to dichotomous outcomes) can only be applied with individual patient data from the original trials, which are often inaccessible to many systematic reviewers and other stakeholders.

There have been efforts to develop core outcome sets (ie, a standardized set of outcomes that should be collected in all new trials), for many disease areas, including asthma.[6] However, adoption of core outcome sets is still somewhat limited and depends heavily on the disease area.[7] For some disease areas, there are dozens of published core outcome sets, resulting in the same problem on a different scale.

How Do We Get There?

Much of the improvement in the collection of HRQoL and other PRO data can likely be attributed to guidelines from regulatory and reimbursement agencies, as well as encouragement from professional societies such as the American Society of Clinical Oncology.[8-10] Although guidance from regulatory and reimbursement agencies may help to standardize outcome collection across trials, it would be burdensome to generate specific outcome guidance for every disease area. Conversely, creating broad guidance might limit relevance of the outcomes to the specific condition of interest.

> Without specific guidance from regulatory and reimbursement agencies, trial sponsors may have difficulty determining the best, most relevant outcomes to collect.

Some regulatory agencies have established programs to promote up-front communication between sponsors and regulatory agencies, allowing them to provide guidance on the collection of PROs early on in trial design. As regulatory and HTA agencies increase patient engagement initiatives, patient organizations have the opportunity to encourage the use of core outcome sets developed with patient involvement. Patient organizations can also influence the uptake of core outcome sets through involvement with clinical guideline development or directly with trial sponsors.[7]

> Increased interest in the patient perspective reinforces the need to treat patient-reported outcomes as a core component of evidence generation.

Encouragement from professional societies may influence outcome collection, but without the same kind of authority as regulatory and reimbursement agencies, these types of initiatives may fall short. Without specific guidance from these agencies, trial sponsors may have difficulty determining the best, most relevant outcomes to collect. Conducting literature reviews early on in trial design may be an efficient method to identify relevant core outcome sets, PRO measures regularly used in similar trials, and information about the validity, reliability, clinical significance, and ability to detect meaningful change using those PRO measures. This information can also be utilized in regulatory and reimbursement submissions to facilitate the agency's review of the instrument.

What Are the Practical Implications for HTA Submissions?

Although these results are specific to CDA-AMC reviews, other HTA agencies have their own patient engagement initiatives, indicating that PROs and the patient experience are of increasing interest across agencies. In addition, submissions to various HTA agencies typically utilize data from the same registrational trials, meaning that increased levels of patient engagement across HTA agencies are working synergistically to yield additional PRO data to inform reimbursement decisions beyond the Canadian context.

Pragmatically, this increased interest in the patient perspective reinforces the need to treat PROs as a core component of evidence generation. Because HTA dossiers in multiple jurisdictions often draw from the same registrational program, early, deliberate selection of PRO instruments (including consideration of existing core outcome sets where available) can improve cross-trial comparability. In the submission itself, clearly articulating the rationale for the selected concepts and instruments, linking them to the outcomes that patients say are most important, and prespecifying how PRO data will be analyzed and contextualized alongside clinical endpoints can support more transparent benefit–risk and value discussions during HTA review, even when clinical outcomes may appear similar across treatments.

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Predicting PICOs Under EU Joint Clinical Assessment: Is One Method Enough?

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KEY TAKEAWAYS

The European Union's new Joint Clinical Assessment summarizes evidence on the relative clinical effectiveness and safety of a health technology to inform pricing and reimbursement decisions for all member states.

Health technology developers can gain an advantage by anticipating JCA expectations for population, intervention, comparator, and outcomes (PICO) when planning their evidence generation.

During ISPOR Europe 2025, a panel of experts explored different strategies for PICO prediction to determine if there is a single best method or if a blended strategy is preferable.

The new European Union (EU) Health Technology Assessment (HTA) Regulation (EU 2021/2282) marks one of the most significant changes in European market access in recent decades. The new process, launched in 2025, requires oncology and advanced therapy medicinal products (ATMPs) to undergo Joint Clinical Assessments (JCAs) at the EU level, followed by orphan medicines in 2028 and all new medicinal products by 2030. For the first time, a single clinical assessment will help inform pricing and reimbursement decisions across all EU Member States.

JCA is conducted in parallel with the existing assessment process used by the European Medicines Agency (EMA) to recommend marketing authorization by the European Commission. The JCA report created at the end of each assessment, which summarizes the evidence on the relative clinical effectiveness and safety of a health technology, is intended to help national Member State authorities make more timely, efficient, and informed decisions about allocation of healthcare resources.

> Misalignment of evidence package submission with final PICOs required for Joint Clinical Assessment could result in costly rework, weak evidence supporting, and/or delays to access.

At the heart of the JCA process lies PICO (Population, Intervention, Comparator, and Outcomes), factors that comprise the framework within which health technology developer (HTD) submissions are assessed. Every JCA goes through a scoping process to specify PICOs that reflect the requirements of the individual Member States, but these are rarely consistent across countries. Subpopulations differ, comparators evolve and vary across dynamic treatment landscapes, and clinical outcomes may be interpreted differently by national HTA agencies. Consequently, HTDs' ability to anticipate PICOs before the JCA scoping phase could profoundly shape the evidence strategies, trial design alignment, and dossier complexity.

During ISPOR Europe 2025, panelists from academia, industry, and HTA bodies explored different strategies for PICO prediction and considered a critical question: Is there one best method, or is a blended strategy the only practical path forward?

This article will present the highlights of that discussion, including an overview of the strengths and limitations of the various strategies. It will also outline key practice-informed early lessons from the first year of JCA implementation that can help HTDs navigate the JCA process.

The Regulatory Shift: From National to EU-Level Assessment

Historically, HTA requirements have varied significantly across individual EU Member States. The EU HTA Regulation introduces a structured, permanent joint framework designed to harmonize clinical assessments across the Member States (while reducing duplication), enhance transparency, and accelerate patient access to innovative therapies in Europe.

Why it matters:

- It establishes a single EU-level submission for clinical assessment.
- It is closely aligned with EMA timelines, with scoping starting early, often before full regulatory clarity (eg, changes to the Summary of Product Characteristics [SmPC] may occur during the EMA process, as mentioned in the next section).
- It has the potential to streamline market access and minimize delays in reimbursement decisions, and
- It raises the stakes: Misalignment of evidence package submission with final PICOs could result in costly rework, weak evidence supporting, and/or delays to access.

The complicated process of harmonizing clinical assessments across all member states, in turn, increases the complexities of establishing consolidated PICOs to facilitate those assessments. It also creates challenges for health technology developers trying to anticipate those PICOs and plan their evidence generation accordingly.

- **PICO variability across Member States:** Heterogeneity in how Member States define patient groups, comparators, and outcomes leads to significant variation in PICOs. This variability makes the consolidated PICOs difficult to predict and creates substantial uncertainty for HTDs when planning evidence generation, particularly because national needs and requirements often differ across Member States.
- **Potential change of SmPC:** Recent academic research indicates that up to 33% of ATMPs undergo indication changes during the EMA regulatory process, which could affect the JCA scoping process. These adjustments require rapid adaptation to PICO definitions, potentially affecting trial alignment.
- **Evidence generation challenges for specific health technologies:** Products such as oncology therapies, orphan drugs, and gene therapies face persistent evidence challenges—from rapidly evolving standards of care (eg, oncology) to small trial populations, ethical barriers to randomized controlled trials, and greater reliance on heterogeneous real-world data (eg, orphan drugs/ATMPs). These hurdles create significant uncertainty in meeting JCA evidence expectations.
- **Insufficient resource allocation:** The harmonized assessment process will require HTDs to allocate resources efficiently to meet the demands of both regulatory and HTA evaluations. In particular, the JCA process demands extensive and detailed data and, therefore, requires significant resources and coordination due to the tight deadlines for dossier submissions.

Sources of evidence for early PICO formulation include:

- Draft SmPC and clinical overview (Marketing Authorization Application file)
- EU and non-EU clinical guidelines
- HTD-driven PICO surveys among Member States
- Reimbursement/HTA documents for products approved in the indication for which PICOs are defined
- JCA guidance documents on scoping and outcomes

Methods for Predicting PICOs: Strengths and Limitations

As the EU HTA framework moves from concept to implementation, HTDs are increasingly exploring methods to anticipate likely PICOs before the formal JCA scoping phase. Early prediction can help align clinical development, evidence generation, and value demonstration strategies with anticipated assessment requirements. However, no single methodology currently offers a complete solution.

Traditional approaches such as systematic literature reviews and country-level consultations remain widely used but are often resource-intensive and time-consuming. At the same time, emerging data-driven and artificial intelligence-supported tools (eg, NAVLIN AI PICO Planner) are being explored to accelerate and standardize early PICO identification. In practice, many organizations are considering whether a single method is sufficient or whether a blended approach may provide a more robust strategy.

Table 1 summarizes commonly used approaches for early PICO prediction and highlights their key strengths and practical limitations.

Table. Strengths and Limitations of Commonly Used PICO Prediction Methods

METHOD	STRENGTHS	LIMITATIONS
Systematic Literature Reviews	• **Traditional gold standard** – Systematic approach and widely accepted • **Comprehensiveness & Breadth** – Broad criteria for searches to safely capture all relevant studies for JCA scope	• **Resource** – highest resource use, requires human involvement in screening/identifying relevant PICO • **Timing** – lengthy process in general; also, JCA SLRs need to be conducted within 3 months of submission and for novel therapies, published documentation may not be available at that time
Country PICO Surveys	• **Resemblance** – Closely mimics the actual process from JCA • **Involvement** – Country affiliates can often interact with national HTA bodies and predict what their response to JCA will be	**Resource** – higher resource use, requires response from regional affiliates from each Member State and additional analyses during the consolidation process
AI Based Tools: eg, NAVLIN's PICO Planner	• **Efficiency & Speed** – Generates draft PICOs in weeks vs lengthy SLRs/surveys • **Consistency & Breadth** – Standardized, evidence-based view across sources • **Hybrid Validation** – AI outputs refined with expert review for accuracy	• **Retrospective Nature** – Relies on existing HTA and guideline data, which may not capture novel or emerging evidence • **Interpretability & Transparency** – AI-derived PICOs may need extra explanation to build stakeholder confidence vs expert-driven SLRs
Blended Approach	• Flexible; triangulates insights	• Requires governance and methodology

AI indicates artificial intelligence; HTA, health technology assessment; JCA, Joint Clinical Assessments; PICO, population, intervention, comparator, and outcomes; SLR, systematic literature reviews.

Implications for Industry Stakeholders

- Incentive to predict PICOs early and incorporate into clinical trial program, but risk if misaligned
- Early strategic evidence planning to support both regulatory and HTA/payer needs (eg, 12-18 months pre-JCA submission)
- Evidence generation may need to become modular and adaptive
- Resource allocation decisions may shift from "1 trial = 1 PICO strategy" to "1 trial = multiple PICO contingencies"
- The question of which PICO prediction method is best for JCA is less a question of "either/or" but "when and how much", as all approaches require resources, especially if done repeatedly, to stay up to date
- The EU HTA Regulation requires HTDs to be overinclusive in their PICO scenario planning to prepare for contingencies
- An earlier (joint) agreement on the PICO scope would help mitigate this burden

Implications for HTA Stakeholders in Member States

The JCA is intended to inform pricing and reimbursement decisions in each Member State, and each nation has representatives on the HTA Coordination Group that works with stakeholder groups to jointly define the scope of JCA reports, including PICOs. The HTA agencies from each Member State will want to ensure the PICOs in each JCA meet their nation's specific clinical and economic needs, which will involve some of the same prediction methods used by health technology developers.

Implications for HTA agencies include:

- Requires a balance between flexibility and standardization
- Need for efficient handling of subpopulations and comparators
- Expressing clear expectations (eg, through joint scientific consultations between health technology developers and JCA advisors) will be essential
- Opportunity to evaluate emerging prediction methodologies
- Role in building validation frameworks, especially for AI solutions
- Can serve as neutral domain experts during discussions of comparator relevance
- The challenge will spur innovation in the method of generating and synthesizing evidence
- The pressure of JCA will drive a tighter integration of HTA and value planning in the development of health technologies.

Panelists' Perspective

The transition to EU-level HTA moves beyond coordination and redefines strategic evidence planning. The scoping phase, historically seen as procedural, is now a pivotal decision point that influences trial outcomes, evidence strategy, and resource allocation. Many companies are beginning to treat PICO prediction as an early phase activity rather than a postregulatory task.

> Many companies are beginning to treat PICO prediction as an early phase activity rather than a postregulatory task. However, consolidating PICOs is not straightforward.

However, consolidating PICOs is not straightforward. Member States differ in treatment practices and clinical guidelines, leading to divergent views. A flexible and evidence-based strategy for PICO prediction appears preferable, but the exact methodology remains unclear.

Key takeaways from the ISPOR Europe panel included:

- **Early PICO prediction matters.** All panelists agreed that early prediction of PICO elements is vital. This enables HTDs to initiate and plan evidence generation sooner, reducing the risk of gaps and delays later in the process. No single methodology for PICO prediction currently offers a complete solution; rather, hybrid approaches may be needed.
- **Continuous learning and adaptation.** The JCA process is new for everyone, and early implementation will bring challenges. Applying lessons quickly will be key to building confidence and improving efficiency.
- **A shared commitment to success.** Stakeholders across the board want the EU HTAR and JCA to succeed—not just as a regulatory milestone, but to deliver faster and broader access to innovative medicines for patients across Europe.
- **Collaboration is critical.** Strong collaboration among regulators, HTA bodies, and industry will be essential. In particular, HTDs suggest that more proactive engagement between them and the Member State HTA Coordination Group (established by the Regulation) can help ensure evidence generation aligns with evolving requirements.

The First Year: The Consultant Perspective

From the perspective of the consultancy supporting HTDs, the first year of JCA implementation has served as a learning and adaptation phase for both industry stakeholders and assessors. Working closely with companies across multiple JCAs has underscored the critical importance of early strategic planning, evidence alignment, and clear articulation of clinical value at the EU level.

While companies continue to navigate evolving expectations and operational complexity, the first year has also demonstrated opportunities to embed JCA considerations earlier in development and evidence-generation plans. These early lessons reinforce the need for continued methodological clarification and practical guidance by the HTA Coordination Group to help translate JCAs into efficient and meaningful national HTA and access outcomes.

In particular, the first year of JCA implementation has highlighted several critical success factors for navigating the EU HTA Regulation effectively:

- **Tailor PICO prediction approaches by therapeutic area or timing.** In practice, the most effective strategy

for anticipating PICOs may involve combining multiple approaches and tailoring them to the therapeutic context or stage of development.

  - For example, in therapeutic areas such as oncology, where standards of care evolve rapidly and comparator landscapes differ across Member States, faster approaches such as AI-based tools can help identify likely comparators and patient subpopulations early in development. These early insights can then be validated through systematic literature reviews closer to submission, when more published evidence becomes available.
  - For rare disease areas, PICO surveys with country affiliates or external validation with key opinion leaders and healthcare professionals may add more value than AI-based tools that rely primarily on retrospective evidence.
  - Similarly, when a drug is in the early development phases (phase I or phase II), AI-based tools can support competitive landscape analysis and help identify potential PICOs. As the product progresses into phase III, PICO surveys and systematic literature reviews can further support the development of evidence-based PICOs aligned with anticipated JCA requirements.

- **Allocate appropriate budget and resources early.** Preparing a robust JCA dossier is highly resource-intensive and evidence heavy, requiring substantial cross-functional input, analytical rigor, and coordination across global and European teams. Under-resourcing JCA preparation risks downstream inefficiencies and limits the ability to respond effectively to assessor questions within compressed timelines.
- **Establish clear governance, operating models, and realistic expectations.** Successful JCA execution requires early definition of governance structures, decision-making accountability, and roles across global, regional, and local teams. Managing internal expectations, particularly around timelines, flexibility, and the relationship between JCA outputs and national HTA needs, has emerged as critical to maintaining alignment and momentum.

> While companies continue to navigate evolving expectations and operational complexity, the first year has also demonstrated opportunities to embed JCA considerations earlier in development and evidence-generation plans.

- **Plan evidence strategically and early to enable execution.** Early and proactive evidence planning, aligned with anticipated JCA scope and comparators, is essential. The first year has underscored the importance of embedding JCA considerations into clinical development and evidence-generation plans well in advance, allowing sufficient time for PICO assessment, data readiness, analyses, and dossier development.
- **Leverage external expertise to support strategic positioning.** Involving external experts (including clinical experts, health economics and outcomes research (HEOR) experts, and HTA-experienced advisors) can enhance the robustness, credibility, and clarity of JCA submissions. External perspectives can also help challenge assumptions and strengthen value narratives for a multistakeholder assessment environment.
- **Balance broad cross-functional collaboration with agility in decision making.** While effective JCA preparation requires close collaboration across clinical, regulatory, HEOR, market access, and legal teams, the first year has shown the importance of remaining agile. Clear escalation pathways and decisive leadership are essential to avoid delays and ensure timely alignment on evidence strategy and responses.

Closing Remarks

The HTA Regulation represents a transformative shift toward harmonization and equity in patient access. While the journey will require flexibility and collaboration, the potential benefits (eg, greater consistency, transparency, and speed) make this an exciting time for the HEOR field.

Overcoming Challenges to Innovation in Alzheimer and Parkinson Disease

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KEY TAKEAWAYS

Despite recent regulatory approvals, Alzheimer and Parkinson therapies face significant innovation and reimbursement challenges, particularly for disease-modifying treatments.

Biological complexity, access challenges, and high clinical-trial failure rates hinder research and development progress in both diseases.

Payers can play a crucial role in driving innovation by adopting broader value assessments, flexible reimbursement models, and investing in healthcare infrastructure.

Alzheimer disease and Parkinson disease are two of the most prevalent and burdensome neurodegenerative conditions worldwide. Alzheimer disease accounts for between 60% and 70% of global dementia cases, while the prevalence of Parkinson disease has doubled over the past 25 years, affecting 8.5 million people in 2019. Both conditions are chronic, progressive, potentially life-limiting, and responsible for a significant and increasing burden on health systems, individuals, carers, and society due to aging populations.

Despite significant investment in neuroscience research, most approved treatments today are limited to symptomatic relief. In recent years, some novel amyloid-targeting, disease-modifying therapies in Alzheimer disease and adjunctive symptomatic treatments in Parkinson disease have received regulatory approval. However, innovation in these areas remains limited, with few disease-modifying options available.

Beyond scientific and regulatory barriers, reimbursement has also emerged as a critical challenge: several approved therapies have secured only limited coverage in the United States, while decisions in the European Union and United Kingdom have been negative or remain pending. Therefore, understanding both the barriers to innovation and the key drivers of reimbursement are essential to identifying targeted actions and engaging healthcare payers in transforming the treatment landscape.

Promises and Pitfalls in Recent Therapeutic Advances

Recent advances in Alzheimer disease have focused primarily on amyloid-targeting therapies. However, access remains limited due to safety concerns and reimbursement challenges. **Table 1** summarizes key Alzheimer disease therapies recently appraised by US and European regulatory agencies, together with key issues raised as concerns that later impacted access to the medications.

Lecanemab demonstrated clinical benefit with a 27% slowing in cognitive decline over 18 months compared to placebo and was approved by the US Food and Drug Administration (FDA) in 2023, followed by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) in 2024 and the European Commission in 2025.[1-3] However, despite the MHRA approval, reimbursement remains a challenge, with the English National Institute for Health and Care Excellence (NICE), in its draft guidance, deciding not to recommend lecanemab due to economic model uncertainties, and negative overall cost-effectiveness estimates.[4]

Table 1. Key Alzheimer Disease Therapies Recently Appraised by US and European Regulatory Agencies

Drug Name	Regulatory Status	Key Issues (and agency citing the issue)
Lecanemab	• FDA approval (2023) • MHRA approval (2024) • EMA approval (2025)	Cost-effectiveness concerns (NICE)
Donanemab	• FDA approval (2024) • MHRA approval (2024) • EMA rejection (2025)	Safety Concerns over ARIA (EMA)
Aducanumab	• FDA accelerated approval 2021	Limited evidence of patient benefit resulting in restricted coverage (CMS and commercial payers)

ARIA indicates amyloid-related imaging abnormalities; CMS, Centers for Medicare & Medicaid Services; EMA, European Medicines Agency; FDA, US Food and Drug Administration; MHRA, UK Medicines and Healthcare Products Regulatory Agency; NICE, National Institute for Health and Care Excellence, UK, United Kingdom; US, United States.

Donanemab, another amyloid-targeting therapy, has faced similar challenges. While it was approved by the FDA and MHRA in 2024,[5,6] the European Commission initially rejected its marketing authorization application in March 2025 due to the European Medicines Agency's (EMA's) safety concerns related to amyloid-related imaging abnormalities; after further assessment, the EMA concluded the benefits of the therapy outweighed the risks, and the European Commission granted marketing authorization in September 2025.[7] Both donanemab and lecanemab carry boxed warnings for amyloid-related imaging abnormalities.

Meanwhile, aducanumab received FDA accelerated approval in June 2021, and was subsequently covered in a restricted manner by US public (eg, Centers for Medicare & Medicaid Services [CMS]) and commercial payers, but was still widely criticized by the Institute for Clinical and Economic Review for insufficient evidence of patient benefit and the need for further studies.[8] In January 2024, Biogen discontinued aducanumab's development, reprioritizing their resources towards other Alzheimer disease development projects.[9]

In Parkinson disease, no therapies have yet been shown to slow disease progression, with recent efforts focused on symptom management. For example, the combination therapy foscarbidopa and foslevodopa, given as a 24-hour subcutaneous infusion, was approved by the FDA in 2024 for advanced Parkinson disease.[10] Other recent therapies include opicapone[11] and istradefylline,[12] which are used as adjuncts to levodopa during "off" periods, when patients experience motor symptoms while taking their usual treatment.

Looking ahead, research and development (R&D) pipelines remain active and contain potential future therapies for both diseases. **Table 2** summarizes the current clinical trial landscape in Alzheimer disease and Parkinson disease as of 2024, with 164 active clinical trials investigating drugs for Alzheimer disease, including those targeting prevention and symptomatic relief.[13] This included 48 phase 3, 90 phase 2, and 26 phase 1 trials, with 11 long-term extensions. Most (76%) targeted disease modification, while others focused on neuropsychiatric symptom relief (13%) or cognitive enhancement (12%).[13] Compared with 2023, there was a slight decline in trials and novel compounds, highlighting ongoing challenges and high failure rates in Alzheimer disease drug development.[13]

Table 2. Alzheimer Disease and Parkinson Disease Clinical Trial Landscape in 2024

Disease	Total Active Trials	Therapeutic Goal	Clinical Trial Stages
Alzheimer Disease	164	• 76% disease modification • 13% neuropsychiatric symptoms • 12% cognitive enhancement	• 48 phase 3 • 90 phase 2 • 26 phase 1 • 11 long-term extensions
Parkinson Disease	136	• 55% symptomatic treatment • 45% disease modification	• 58% phase 2 • 12% phase 3

Similarly, as of January 2024, 136 active clinical trials were ongoing in Parkinson disease, with 55% focused on symptomatic treatment and 45% aimed at modifying disease progression.[14] Most (58%) were in phase 2, assessing short-term safety and preliminary efficacy, while only 12% had reached phase 3, with just 3 targeting disease modification.[14]

Despite these active therapeutic pipelines, progress in Alzheimer disease and Parkinson disease is often limited by high attrition and challenges in demonstrating meaningful functional benefits for patients and payers. **Tables 3 and 4** illustrate examples of late-stage failures, including reasons for discontinuation across both conditions.

Why Innovation Is Slow in Neurodegenerative Disease

Innovation in neurodegenerative diseases is limited by biological complexity, methodological barriers, and high clinical-trial failure rates. Both Alzheimer disease and Parkinson disease are heterogeneous, slowly progressive conditions, which makes early diagnosis and trial patient selection difficult. Identifying meaningful endpoints is also challenging, particularly in the early stages where symptoms evolve gradually and are hard to quantify. One such example in the case of Alzheimer disease is early episodic memory decline, which evolves slowly and is difficult to capture reliably with current cognitive endpoints. Even when clinical benefits are observed, they may be modest and difficult to translate into functional improvements that resonate with patients and/or payers. For example, modest improvements in Parkinson disease motor scores, particularly those considered to be below or near the minimally clinically important difference, may not translate into functional benefits that meaningfully improve daily life or justify reimbursement.

High R&D development costs and long development timelines further compound these barriers. Demonstrating meaningful impact often requires large-scale, long-duration trials, yet uncertainty around long-term outcomes and limited windows for market exclusivity increase the financial risk for developers. Without clear signals from regulators and reimbursement authorities, manufacturers often hesitate to invest in this space, with market access challenges being a key barrier to innovation.

Market Access Challenges as an Innovation Bottleneck

Even when therapies achieve regulatory approval, securing reimbursement and market access in Alzheimer disease and Parkinson disease remains complex due to clinical uncertainties, economic constraints, and healthcare system capacity limitations. The slow and variable progression of these diseases, combined with limited evidence of sustained functional improvement, makes it difficult to demonstrate value in payer assessments. In addition, the long-time horizon required to observe clinical benefit poses an additional challenge for payers, particularly in systems where patients transition from commercial insurance to public coverage (eg, Medicare), reducing financial incentives for early investment.

Table 3. Example Late-Stage Failures in Alzheimer Disease Drug Development

Drug Name	Company	Mechanism of Action	Reason for Failure
Gantenerumab	Roche / Genentech	Anti-amyloid β monoclonal antibody	Failed phase 3; no clinical benefit[a]
Solanezumab	Eli Lilly	Targets soluble amyloid β	Phase 3 A4 study showed no cognitive benefit in preclinical Alzheimer disease (elevated brain amyloid levels but no clinical symptoms of disease)[b]
Semorinemab	Genentech / AC Immune	Anti-tau monoclonal antibody	Failed phase 2; no efficacy in slowing progression[c]
Simufilam	Cassava Sciences	Oral small molecule targeting filamin A	Failed phase 3; did not meet primary endpoints[d]

[a] [Ad hoc announcement pursuant to Art. 53 LR] Roche provides update on Phase III GRADUATE programme evaluating gantenerumab in early Alzheimer's disease [news release]. Roche. https://www.roche.com/media/releases/med-cor-2022-11-14. Published November 13, 2022. Accessed March 6, 2026.
[b] Lilly Provides Update on A4 Study of Solanezumab for Preclinical Alzheimer's Disease [news release]. Lilly. https://investor.lilly.com/news-releases/news-release-details/lilly-provides-update-a4-study-solanezumab-preclinical. Published March 8, 2023. Accessed March 6, 2026.
[c] Teng E, Manser PT, Pickthorn K. Safety and efficacy of Semorinemab in individuals with prodromal to mild Alzheimer disease: a randomized clinical trial. JAMA Neurol. 2022;70(8):758-767. doi:10.1001/jamaneurol.2022.1375.
[d] Cassava Sciences Topline Phase 3 Data Did Not Meet Co-Primary Endpoints [press release]. Filana Therapeutics. https://www.filanatx.com/news-releases/news-release-details/cassava-sciences-topline-phase-3-data-did-not-meet-co-primary. Published November 25, 2024. Accessed March 6, 2026.

Table 4. Example Late-Stage Failures in Parkinson Disease Drug Development

Drug Name	Company	Mechanism of Action	Reason for Failure
Prasinezumab	Roche / Prothena	Anti-α-synuclein monoclonal antibody	Phase 2b trial failed to meet primary endpoint[a]
Minzasolmin	UCB / Novartis	α-synuclein aggregation inhibitor (oral)	ORCHESTRA phase 2 study failed all endpoints[b]
Risvodetinib	Inhibikase Therapeutics	c-Abl tyrosine kinase inhibitor	Phase 2 trial failed to show significant functional benefit[c]
Solengepras	Cerevance	GPR6 inverse agonist	Phase 2 trial failed to meet primary endpoint[d]

[a] Roche's Phase IIb study of prasinezumab missed primary endpoint, but suggests possible benefit in early-stage Parkinson's disease [news release]. Roche. https://www.roche.com/media/releases/med-cor-2024-12-19. Published December 18, 2024. Accessed March 6, 2026.
[b] Findings from minzasolmin proof-of-concept ORCHESTRA study shape next steps in UCB Parkinson's research program [press release]. UCB. https://www.ucb.com/newsroom/press-releases/article/findings-from-minzasolmin-proof-of-concept-orchestra-study-shape-next-steps-in-ucb-parkinson-s-research-program. Published December 16, 2024. Accessed March 6, 2026.
[c] Manalac T. Inhibikase scraps Parkinson's drug after disappointing mid-stage data. BioSpace. https://www.biospace.com/drug-development/inhibikase-scraps-parkinsons-drug-after-disappointing-mid-stage-data. Published January 30, 2025. Accessed March 6, 2026.
[d] Cerevance's Solengepras fails primary endpoint in phase II Parkinson's trial, shows promise for non-motor symptoms. MedPath. https://trial.medpath.com/news/c4ee4baf02901a2c/cerevance-s-solengepras-fails-primary-endpoint-in-phase-ii-parkinson-s-trial-shows-promise-for-non-motor-symptoms. Accessed March 6, 2026.

Clinical trials often rely on surrogate biomarkers—such as amyloid beta clearance in Alzheimer disease—but their relevance to patient outcomes remains controversial. While some regulators have accepted these endpoints, they are not consistently recognized by health technology assessment bodies and payers. In Parkinson disease, innovation is hampered by the absence of validated biomarkers to assess disease-modifying effects. Even when clinical benefits are observed, they may be modest and difficult to translate into functional improvements that resonate with payers.

In Alzheimer disease, payer skepticism around disease-modifying therapies persists. For example, the CMS requires clinicians to submit data to a CMS-facilitated registry when administering FDA-approved anti-amyloid drugs, as a condition of Medicare coverage.[15] Meanwhile, NICE's draft guidance not to recommend lecanemab highlighted concerns over cost-effectiveness that were partly driven by the uncertainty around long-term benefits.[4]

Healthcare system readiness and infrastructure requirements (such as diagnostic imaging, infusion delivery, and ongoing monitoring) pose additional challenges, as many healthcare systems are not set up to support the delivery of such services. This lack of preparedness further complicates reimbursement decisions and ultimately hinders the development and adoption of such therapies.

Scientific uncertainty and market access barriers form a reinforcing cycle that continues to slow progress in Alzheimer disease and Parkinson disease, making it difficult for promising therapies to reach patients despite significant research investment.

How Payers Can Incentivize Innovation

To encourage progress in Alzheimer disease and Parkinson disease, healthcare systems should consider how they can play a role in incentivizing development. Traditional quality-adjusted life year-based economic models do not fully capture all possible broader value elements that are particularly important in neurodegenerative disease treatments.[16,17] For example, impacts on the wider family, productivity loss, and hospitalizations are all likely to be particularly important for such therapies. Payers should consider how these broader value elements could be integrated into assessments, as they are particularly relevant for aging populations, where societal costs often exceed clinical costs. Additionally, greater alignment of evidence requirements between regulators and payers may also improve access.

In addition to reconsidering how value is measured, innovative pricing models, such as outcome-based agreements and indication-specific pricing, could be considered to align payment with real-world impact. For high-cost therapies with uncertain benefits, installment-

based payments or coverage with evidence development can reduce payer risk while maintaining patient access.

Importantly, investment in the disease registries and data platforms that support these flexible reimbursement mechanisms could also support both R&D and postapproval, real-world evidence generation. Additionally, investment in strengthening other key infrastructure such as biomarker testing, imaging, and infusion facilities will be important for enabling timely access.

It is important that governments recognize the importance of innovative strategies to improve reimbursement and access for these therapies. For example, consider higher premiums for disease-modifying therapies than for therapies that provide only symptomatic relief. Lessons from other therapy areas, such as oncology,[18] could also be leveraged where initiatives such as the Cancer Drugs Fund in England have helped turn the tide in terms of the lack of innovation beyond chemotherapy.

Payers can play a key role in advancing innovative treatments for Alzheimer disease and Parkinson disease by embracing a mindset that is less skeptical and more strategic. Payer support for broader value assessment frameworks, flexible reimbursement policies, and real-world data repositories is crucial to fully realizing the potential of future therapies for these populations.

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Addressing Barriers to Timely and Equitable Access in Oncology: The Case of Individualized Neoantigen Therapies

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KEY TAKEAWAYS

Unlike advanced therapies that target rare diseases, individualized neoantigen therapies have the potential to treat a larger patient population, particularly those in the earlier stages of cancer.

The unique characteristics of these advanced therapies may not be adequately addressed by existing payment models.

To ensure timely access while maintaining the financial sustainability of healthcare systems, there is a need to address the inherent limitations of current funding mechanisms and explore alternative approaches.

Nearly 6.2 million cancer deaths in the European Union and 1.3 million in the United Kingdom are estimated to have been prevented between 1989 and 2024, driven by reductions in risk factors, advancements in early detection, and significant progress in cancer management and therapy.[1] Among the therapeutic innovations, precision medicine and advanced genetic and molecular technologies have demonstrated substantial improvements in survival and patient quality of life.[2] However, as seen with the introduction of multi-indication medicines, healthcare systems must continuously adapt to ensure appropriate access to these therapies while managing their associated financial and logistical complexities.[3-4]

> Unlike advanced therapies that target rare diseases, individualized neoantigen therapies have the potential to treat a larger patient population, particularly those in the earlier stages of cancer.

A key innovation in this landscape is the development of individualized neoantigen therapies (INTs).[5] Designed to tailor treatment to each patient's unique molecular tumor profile, INTs target specific neoantigens (proteins arising from tumor-specific mutations). This highly personalized approach could change future cancer care, offering potentially more effective and durable responses across a wide range of indications.[6]

Barriers to Access for Innovative Oncology Therapies

Novel oncology therapies often face barriers at launch due to financial constraints and uncertainties about their long-term clinical benefits. For instance, cell and gene therapies typically involve high upfront costs, yet the full scope of their effectiveness may take years to materialize.[7] This delay may create uncertainty for payers and therefore complicate the assessment of their true value for healthcare systems, hindering patient access.[8]

The formal methodologies of cost-effectiveness analysis, often required early in health technology assessment (HTA) for reimbursement, add complexity to evaluating new therapy platforms. Often, short-term clinical evidence fails to capture the full value of these innovations, including their potential impact on the healthcare system and broader societal and economic benefits. There is a need for more comprehensive and forward-looking evaluation frameworks to fully recognize the value of novel platforms with the potential for significant scientific spillover effects that could help address a wide range of diseases in the future.

Unique Challenges for INTs

INTs introduce new considerations. Unlike other advanced therapies that target rarer diseases and smaller patient populations, INTs have the potential to treat a larger patient population, particularly those in the earlier stages of cancer, such as high-risk cutaneous melanoma.[5] This wider applicability—while offering the potential to improve clinical outcomes broadly and reduce disease burden at a system level—may also carry broader budget implications for healthcare systems.

Importantly, the fact that INTs may find application in earlier-stage oncology indications introduces an additional layer of complexity for access and reimbursement. In such cases, novel therapies are often approved based on established clinical endpoints—such as disease-free survival (DFS) or recurrence-

free survival (RFS). However, from the perspective of payers and HTA bodies, these endpoints may carry a degree of uncertainty regarding long-term outcomes, which can challenge reimbursement decision making and potentially delay patient access.[9]

Exploring Funding Mechanisms for Enhancing Access

Different funding mechanisms and payment models have been employed across a number of countries, particularly in Europe and the United Kingdom, to ensure timely access and reimbursement for innovative therapies in oncology. These approaches are not routinely applied for all submissions and remain the exception rather than the rule. A notable example is chimeric antigen receptor T-cell (CAR-T) therapies, which have been made accessible through financing approaches such as coverage with evidence development (CED) and performance-linked payment models.

Although CAR-T therapies are frequently referenced in discussions about innovative payment models, they differ from INTs in important ways. Due to their early oncology-stage indication and broader patient eligibility, INTs exhibit unique characteristics that may not be adequately addressed by existing payment models—highlighting the need to address the inherent limitations of current funding mechanisms and explore alternative approaches to ensure timely access.

The following provides a brief overview of these mechanisms, along with their potential for improvement. Additionally, **Table 1** summarizes how current funding mechanisms address key considerations in ensuring timely access to INTs, along with their associated limitations.

Coverage With Evidence Development

France and England have employed CED models to facilitate access to CAR-T therapies for hematologic malignancies while additional evidence is collected to resolve assessment uncertainties.[10,11]

France implemented a CED approach with annual HTAs, alongside an early access model (formerly the Autorisation Temporaire d'Utilisation, now the Autorisation d'Accès Précoce). As part of this program, manufacturers must collect real-world safety and efficacy data on patients who receive early access to the therapy, and this information is used subsequently to complement clinical data from pivotal trials to inform HTA and reimbursement decisions. Clinical outcomes are also collected at specific intervals to inform HTA assessments; for therapies like tisagenlecleucel (Kymriah®) and axicabtagene ciloleucel (Yescarta®), these outcomes included survival rates, remission status, disease progression, and adverse events. This data collection was managed by the Lymphoma

Table 1. Applicability of current funding mechanisms for INTs

FUNDING MECHANISMS		CHALLENGES TO TIMELY ACCESS FOR INTS			
Mechanism Types	**Example of Scheme (Country)**	**Budget Impact Addressed? (Yes/No/Partially)**	**Endpoint Uncertainty Addressed? (Yes/No/Partially)**	**High Upfront Cost Addressed? (Yes/No/Partially)**	**Long-Term Cost-Effectiveness Addressed? (Yes/No/Partially)**
Coverage with Evidence	Cancer Drugs Fund (England)	Partially. It provides financial certainty through a fixed budget and a mechanism for controlling expenditures	Partially. Data collection period may not be long enough to generate evidence on other endpoints (eg, overall survival). CAR-Ts have been an exception with 5-year funding via CDF	Partially. Commercial arrangements within CDF could address this	Partially. Data collection period may not be long enough to capture potential long-term benefits.
	Early AAP[a]+ annual HTAs (France)	No	Yes. Further data can be collected year after year to help mitigate uncertainty around clinical effectiveness during evaluation by HAS	No	Not applicable[b]
Performance-Linked Payment Models	Outcomes-based staged payments (Belgium, Italy)	Partially. Models limit spending on therapies that miss milestones, but do not directly address budget impact	Yes. Models are based on collection of additional clinical data and aligning payments (or rebates) with therapy performance	Yes	Yes. Assuming new HTAs conducted after agreement, they could generate more robust long-term evidence for cost-effectiveness analyses
	Outcomes-based rebates (Germany)			Partially. Not when payment is made completely upfront and then rebates paid for milestones missed by the therapy	

AAP indicates Access Authorisation Programme; CAR-T, chimeric antigen receptor T-cell therapy; CDF, Cancer Drugs Fund; CEA, cost-effectiveness analysis; HAS, Haute Autorité de Santé (High Authority for Health); HTA, health technology assessment; INTs, individualized neoantigen therapies.

[a] The Early Access Authorisation Programme (AAP) enables manufacturers to set initial prices freely, guarantees funding for the drug for the period of the programme, and includes a subsequent mandatory rebate based on the final negotiated price, balancing early access with cost control.

[b] Not applicable since CEA is not a routine entry requirement for the assessment in the country.

Academic Research Organization and reported quarterly by hospitals.[10]

In England, it was done through the Cancer Drugs Fund (CDF). Since its introduction the CDF has facilitated access to new cancer drugs while further evidence is gathered to address clinical uncertainties identified by the National Institute for Health and Care Excellence (NICE).[11] For Kymriah, a key uncertainty for NICE involved overall survival and the proportion of patients who go on to have a stem cell transplant or require intravenous immunoglobulin after treatment. For Yescarta, a key uncertainty for NICE involved the choice of overall survival extrapolation in the cost-utility analysis, and the resulting uncertainty around the incremental cost-effectiveness ratio.[12]

> Many health systems lack the robust infrastructures needed for real-world evidence collection, which has limited the implementation of coverage with evidence-development funding models.

Opportunities for Improvement.
CED models continue to face significant implementation barriers. Although some health systems have initiated efforts to establish robust infrastructures for real-world data collection, a substantial number of jurisdictions lack the integrated data environments necessary to systematically capture health outcomes and resource utilization.[13] Addressing these deficiencies through the development of interoperable health data platforms and the harmonization of national data governance frameworks will be critical to support rigorous evidence generation and informed decision making.

Performance-Linked Payment Models
Other countries have implemented performance-linked payment models when considering the integration of CAR-T therapies.[12] In Germany, "outcomes-based rebates" have been employed, where the pharmaceutical company provides rebates to the payer based on individual outcomes, such as for patients who die within a (undisclosed) time frame following treatment with Kymriah. In Italy and Spain, "outcomes-based staged payments" have divided the total cost of the therapy into installments linked to patient outcomes, facilitated by national registry systems.[12] Belgium has also adopted a pay-for-performance model, utilizing spread payments to align costs with therapeutic outcomes.[14]

With many stakeholders attracted to the concept of addressing clinical uncertainty by linking payments to specific performance metrics, there is growing consensus on the importance of adopting such innovative payment models. A recent report from the Organisation for Economic Co-operation and Development reveals that 16 of the 28 countries surveyed reported utilizing some form of performance-based managed entry agreement.[15] Notably, Italy has successfully implemented outcomes-based reimbursement through the registry platform of the Italian Medicines Agency, enabling managed-entry agreements for various treatments, with 5 of the first 6 reimbursed Advanced Therapy Medicinal Products (ATMPs) in Italy utilizing such agreements to facilitate patient access.[8]

Another notable characteristic of these models, beyond addressing clinical uncertainty, is the option to facilitate payments in annuity installments, which can help mitigate cash flow and budget impact challenges. Although many stakeholders view the implementation of such payment structures as difficult due to national and EU-level accounting regulations serving as barriers, certain legal provisions in some countries could facilitate their adoption.[16] These provisions have been seen in the context of both ATMP innovative payment models and broader financial reforms, such as the adaptation of budget cycles in Wales, where 3-year periods can be used to support long-term financial planning for innovative therapies,[17] and France's commitment to legislative changes allowing installment payments for advanced therapies.[18]

Opportunities for Improvement.
While these models obviously better align payment and value, they also present challenges. Defining and measuring "performance" across various disease settings can be intricate, and establishing monitoring systems to generate the data needed for financial settlements may require considerable administrative effort.

> Establishing a harmonized framework for performance assessment may be critical for reducing variability, enabling cross-border learning, and facilitating the broader adoption of these models.

The definition of "performance" in these models can vary significantly among countries and among payers, reflecting differences in regulatory frameworks and standards of evidence. This heterogeneity introduces considerable complexity in both the implementation of these models and the comparability of outcomes across healthcare systems. Establishing a harmonized framework for performance assessment may be critical for reducing variability, enabling cross-border learning, and facilitating the broader adoption of these models.

Finally, healthcare systems in which patients have the option of switching between different insurance providers must establish adequate procedures for risk allocation. This is heightened for those targeting non-orphan indications.

Other Proposed Strategies
Beyond the funding mechanisms discussed above, several alternative strategies have been proposed or implemented across different jurisdictions to address barriers to timely access for innovative therapies.

In Germany, 2 distinct models have been proposed. One is a dynamic pricing model—proposed by Techniker Krankenkasse—whereby payers initially cover therapy costs at a regulated price for the first 2 years postlaunch, followed by price renegotiation based on real-world evidence and rebates if effectiveness is unsupported[19]; while this approach is designed to overcome

access delays stemming from clinical uncertainty, the proposed time frame may be insufficient to generate robust evidence to support price negotiations. The second proposed model is a managed market access model, proposed by health insurance provider Barmer, which would restrict prescribing to specially qualified centers for higher-priced drugs with initially limited evidence, while simultaneously conducting application research[20]; this would facilitate quality-assured access and enable additional data collection for a more robust value assessment.

In Greece, a pharmaceutical innovation funding initiative has been proposed to provide transitional compensation for new treatments from EMA approval until inclusion in the national reimbursement list, focusing specifically on ATMPs.[21] While this initiative would facilitate temporary access and additional data collection, it does not involve adjustments to the current value assessment framework, and challenges remain in regard to securing funding amid budget cuts and avoiding bureaucratic delays.

In England, beyond the CDF, the Association of British Pharmaceutical Industries has proposed a rapid entry to the managed access process, whereby NHSE and NICE would collaborate with industry using ATMPs as pilots; this plan would reduce appraisal burdens and streamline the transition to routine commissioning, ensuring timely patient access, although funding challenges and implementation complexity persist.[16] Additionally, the 2024 Voluntary Scheme for Branded Medicines Pricing, Access and Growth—a noncontractual agreement between the UK government, the National Health Service in England, and the Association of British Pharmaceutical Industries—introduces innovative payment mechanisms including outcomes-based agreements that allow for pricing models facilitating immediate reimbursement; challenges remain around data collection and aligning performance metrics with reimbursement models.[22]

Table 2. Evaluation of alternative strategies for the application of INTs

Strategy (country where proposed or implemented)	Description	Access Facilitators	Barriers to Widespread Implementation
Proposed Funding Initiatives from Payers, Policy Makers, or Policy Advisors			
Dynamic pricing model for ATMPs (Germany)	Payers cover ATMP costs at a regulated price for first 2 years; price renegotiation based on real-world evidence.[19]	Overcomes potential access delays due to clinical uncertainty.	Limited time may not generate robust evidence.
Managed market access model for ATMPs (Germany)	Restrict prescription to qualified centers; simultaneous research for higher-priced drugs.[20]	Ensures timely, quality-assured access; collects additional data for robust value assessment.	Limited practical experience so far.
Pharmaceutical innovation funding initiative (Greece)	Transitional funding from EMA approval to national reimbursement for ATMPs.[21]	Facilitates temporary access and data collection for value assessment.	Funding constraints; bureaucratic delays.
Implementation of a rapid entry to managed access process (England)	Streamlined ATMP pilot process with industry collaboration to reduce appraisal burdens and ease transition to routine commissioning.[16]	Ensures timely access; collects additional data.	Funding challenges; implementation complexity.
Pooled interim fund (Australia)	Bridging funding program for early, temporary access to therapies addressing high unmet clinical needs.[23]	Secures temporary access and data collection.	Defining "high unmet clinical needs" can be a complex process.
Negotiation Frameworks and Regional Access Initiatives			
Negotiation frameworks (VPAG, England)	VPAG (England) is a noncontractual agreement for branded medicines. The scheme introduces innovative payment mechanisms, including outcome-based agreements.[22]	Timely access; addresses uncertainty via outcomes-based payment.	Data collection and aligning metrics with reimbursement can be challenging.
Regional agreements for innovation and access (European Union)	Early dialogue, horizon scanning, funding pathways to reduce fragmentation.[24-27]	Promotes equitable, timely access.	Aligning national policies with regional goals; consistent reimbursement across markets.
Other Adopted Strategies			
Cost-effectiveness analysis waiver policy (South Korea)	Exempts oncology and orphan drugs for small patient populations from strict CE thresholds.[28]	Mitigates access hurdles created by strict CE thresholds.	Adapting to prevalent diseases may be complex.

ATMP indicates advanced therapy medicinal products; CE, cost-effectiveness; EMA, European Medicines Agency; INT, individualized neoantigen therapies; VPAG, Voluntary Scheme for Branded Medicines Pricing, Access and Growth.

Australia's HTA Review Reference Committee has recommended establishing a Bridging Funding Program providing early, temporary subsidized access to therapies addressing high unmet clinical needs, ensuring funding aligns with demonstrated benefits; the primary implementation challenge involves the complexity of defining what constitutes "high unmet clinical need" in practice.[23]

> The European Union has been focused on equal access to innovation and competitiveness, with early dialogue mechanisms and funding pathways proposed to minimize fragmentation and complement national-level discussions.

At the regional level, the European Union has been increasingly focused on equal access to innovation and competitiveness,[24-26] with early dialogue mechanisms and funding pathways proposed to minimize fragmentation and complement national-level discussions. Aligning national policies with broader regional goals remains challenging; however, growing political momentum is evidenced by the adoption of more than half of the initiatives outlined in the Draghi report's Competitiveness Compass within one year of its publication.[27]
Finally, South Korea has implemented a cost-effectiveness analysis waiver policy since 2015, exempting anticancer and orphan drugs targeting small patient populations with limited treatment options from strict cost-effectiveness thresholds, mitigating access hurdles, though adapting this model to more prevalent diseases may involve considerable complexity.[28]

Conclusion

The advent of innovative therapy platforms in oncology, such as INTs, presents a significant opportunity to explore solutions that ensure timely access for patients while maintaining the financial sustainability of healthcare systems.

Such solutions also require a framework for evidence creation to support regulatory approval and reimbursement, ensuring sufficient quality to limit uncertainty and support decision making and timely access for cancer patients.

Policy makers, payers, industry stakeholders, and patient groups must engage in constructive dialogue to address barriers and propose policy changes that ensure timely and equitable access to oncology advancements.

Disclosure statement

Mike Hartevelt is an employee of Merck Sharp & Dohme LLC (MSD), a subsidiary of Merck & Co, Inc, Rahway, NJ, USA. At the time of publication of this article, Zine El Abidine Mosbahi is no longer employed by MSD IDEA SPA; however, the work presented in this article was conducted while he was affiliated with the company. Federico Rodriguez-Cairoli and David Tordrup are employees of Triangulate Health Ltd. Triangulate Health Ltd received funding from MSD to conduct the research. Lieven Annemans and Meindert Boysen contributed to the article pro bono without receiving any honoraria.

Data availability

Data used in the paper are proprietary of MSD.

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Advocacy Does Not Stop at Approval: RAAP Amplifies Patient Voices on Battling Real-World Barriers to Access

Michael Eging, Executive and Founder, Rare Access Action Project, Washington, DC, USA

Q&A

"If policy makers are willing to bring in real-world data, the patient voice, and a willingness to compromise, we can arrive at solutions that genuinely benefit patients. That is ultimately the benchmark that should matter."

– Michael Eging

Founded to tackle one of the most persistent blind spots in rare disease policy, the Rare Access Action Project (RAAP) focuses on what happens after US Food and Drug Administration (FDA) approval, when therapies meet the realities of coverage, reimbursement, and real-world access. Led by Executive and Founder Michael Eging, RAAP brings together patient organizations, life sciences leaders, and policy stakeholders to address the structural barriers that can delay or deny treatment to patients who have already waited years for a diagnosis. Shaped by lived experience and grounded in policy expertise, RAAP has become a critical voice in reframing access not as a cost problem, but as the final and decisive step in turning rare disease innovation into patient impact.

PharmaBoardroom: Could you start by introducing RAAP—its mission, positioning, and current policy priorities?

Michael Eging: RAAP is a nonprofit coalition bringing together patient organizations, life sciences stakeholders, and other partners to address access challenges patients face after FDA approval. While many organizations focus on preapproval issues—which are significant—our work concentrates on what happens once a product is approved and patients need real-world access. We focus on state and federal payment and access issues, including Medicare, Medicaid, and other programs.

RAAP began in 2016 as an ad hoc coalition and became a nonprofit in 2018. It started as a grassroots effort with people coming together around shared needs. My involvement is deeply personal: my father died of a rare disease while I was in college. Being able to apply my experience in life sciences to tackle the same questions my family faced—how to access care, what treatments exist, and what a diagnosis truly means—has been particularly meaningful.

That lived experience is reflected across the RAAP team. Many of our staff members have been personally affected by rare disease. We bring not only professional expertise, but a personal understanding of the challenges patients and families face.

PB: You mentioned that FDA approval is just the first step. What are the biggest disconnects between approval and patient access?

ME: The largest disconnect is that much of the healthcare system is structurally designed to say "no." Rare disease therapies require tremendous effort to move from discovery through phases 1, 2, and 3, often with phase 4 commitments. That takes enormous risk, investment, and collaboration. Yet once a therapy receives FDA approval, the response often shifts. Patients face prior authorizations, step therapy, and lengthy formulary reviews. Some therapies can take 18 to 36 months, or longer, to gain access through Medicaid programs.

The dissonance is stark. We invest to demonstrate life-changing benefits, but the postapproval system prioritizes cost containment over access.

PB: How does the fragmentation of the US payer system, across commercial insurance, Medicare, and Medicaid, affect patient access compared with more centralized European systems?

ME: Many rare disease therapies approved in the United States never launch in other markets. Patient populations are extremely small, and navigating the regulatory and access frameworks outside the United States is uncertain. Even in European single-payer systems, innovation does not always translate into access.

> Once a therapy receives FDA approval, it can take 18 to 36 months, or longer, for patients to gain access through Medicaid programs.

For patients in the United States, navigating Medicaid, Medicare, and commercial insurance is complex. Each program has different requirements, and patients often need substantial support. RAAP connects patients with these resources while advocating to address policy barriers.

I saw this first-hand during the launch of a rare pediatric epilepsy therapy. FDA approval was achieved, and children could finally access the treatment. But as we navigated Medicaid, in one state the therapy was routed through an ophthalmology pharmacy and therapeutics (P&T) committee. There were no rare disease specialists involved. The result was a burdensome prior authorization process that discouraged clinicians and families.

These disconnects are common. Some advocacy organizations have strong voices, but many lack resources to sustain advocacy or even alert patients to barriers they will face.

PB: Given the expertise gaps on review committees and the insurance and policy barriers you described, what policy priorities is RAAP focusing on today?

ME: Our priorities focus on removing postapproval barriers. One example is to model legislation requiring states to embed patients and rare disease specialists in decision making. Beyond rare disease advisory councils, this legislation would require P&T committees, drug utilization review boards, or prescription drug affordability boards to include a patient, a patient advocate, and a physician with relevant rare disease expertise **as a voting member** whenever a rare-indicated therapy is under review.

By integrating patients and clinicians into these discussions, we connect scientific and regulatory understanding with lived experience. The result is better-informed coverage decisions and a smoother patient journey beyond FDA approval.

PB: Does patient-led development translate into patient involvement in access decisions?

ME: At RAAP, patients are genuinely at the table. We have a Patient Engagement Caucus that is patient-led, and our state and federal committees are cochaired by life sciences and patient advocates. Many issues originate from the patient caucus and are elevated through that structure.

We support patients through education—webinars, white papers, and outreach. We also bring them to policy maker meetings so they can discuss gaps and potential solutions.

PB: The Orphan Drug Act (ODA) is foundational for rare disease. How does it function in today's environment?

My father died of a rare disease without a treatment. Today, 40-plus years later, the landscape is different. There are therapies even for my father's cancer. A family friend lived nearly 18 months beyond diagnosis, compared with my father's 6 months. That is real progress.

The ODA provided the foundation, but accelerated approval pathways, surrogate endpoints, streamlined clinical programs, and pediatric rare disease vouchers have transformed the development landscape. They allow developers to ask if pursuing a therapy for 200 patients can both impact lives and generate a return on investment.

There are proposals to restrict Medicaid reimbursement for accelerated approval therapies, arguing that evidence is insufficient. In rare disease, particularly ultra-rare conditions, traditional trials may be impossible. These tools exist to deliver life-changing treatments.

> By integrating patients and clinicians into these discussions, we connect scientific and regulatory understanding with lived experience. The result is better-informed coverage decisions and a smoother patient journey beyond FDA approval.

I was involved in launching a gene therapy for spinal muscular atrophy. Historically, many children died before age 2. Today, some are attending kindergarten. This demonstrates that early patient engagement, combined with thoughtful policy and access planning, doesn't just accelerate approval; it ensures therapies actually reach the patients who need them. Going forward,

additional tools, including artificial intelligence-enabled modeling and smarter priority review mechanisms, can further accelerate discovery and improve both outcomes and access.

PB: How far have outcomes-based and risk-sharing payment models progressed in rare disease, and what would it take to scale them meaningfully in the United States?

We operate in a 21st-century system built largely in the 1990s and early 2000s, with remnants from the 1970s and 1980s. That system struggles to absorb personalized therapies.

For rare disease, we need models that stabilize the marketplace and ensure patients can access therapies at FDA approval. Value-based pricing and payment over time, particularly for cell and gene therapies, are increasingly important.

I am especially interested in Medicaid reinsurance and secondary reinsurance markets to stabilize costs. Arizona offers an example. Since the 1990s, the state has led in risk pooling and innovative financing. Rare disease is like a genetic lightning strike, but it is insurable—much like catastrophic events for which insurance models already exist. We need systems that provide the right coverage at the right time.

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Delays can be devastating. Imagine launching a gene therapy and Medicaid takes 24–36 months to decide on coverage. Infants may age out of the label before treatment. Rare disease patients cannot wait. Sustainable access models are critical to ensure research, development, and FDA approvals translate into real patient impact.

PB: To what extent do state-by-state differences in Medicaid coverage create access barriers?

ME: If you have seen one Medicaid program, you have seen one Medicaid program. States operate under different waivers, payment models, coverage criteria, and administrative rules, which creates significant variation in how care is accessed and reimbursed.

Many rare disease patients, particularly pediatric patients who are more likely to rely on Medicaid, must travel across state lines to access centers of excellence. When they do, reimbursement rates, coverage criteria, prior authorization requirements, and drug acquisition costs often differ. That creates an administrative burden for providers and significant exhaustion for patients and families.

There are ongoing discussions about aligning eligibility and access criteria across states, but today the system remains a patchwork. That fragmentation is a material barrier to access and a major source of burden for the rare disease community.

PB: What other topics need to be further emphasized?

One area I would emphasize is the growing uncertainty patients face as a result of recent policy initiatives. Between the Inflation Reduction Act, proposed fixes in Congress, state-level price control mechanisms, and most-favored nation pricing, we are seeing real instability in coverage. A patient who has access today may not have access tomorrow.

> If you have invested years of scientific effort, human capital, and patient participation to bring a therapy to market, it makes no sense for access to become the next battleground without the patient voice present.

We need to step back and re-orient the discussion around long-term solutions that provide certainty of coverage. If patients are placed at the center of these conversations, it is possible to lower out-of-pocket costs while maintaining a viable marketplace for plans and manufacturers and managing risk in rare disease coverage.

There are constructive paths forward, but they require collaboration rather than political point-scoring. If policy makers are willing to bring in real-world data, the patient voice, and a willingness to compromise, we can arrive at solutions that genuinely benefit patients. That is ultimately the benchmark that should matter.

PB: What is your final message?

ME: Pharmaceutical executives already know rare disease patients well through development programs, clinical trials, and FDA engagement. These patients are informed, articulate, and deeply invested in their therapies.

Once a drug is approved, I would strongly encourage companies to support and empower those patients to stay involved. Advocacy does not stop at approval. If you have invested years of scientific effort, human capital, and patient participation to bring a therapy to market, it makes no sense for access to become the next battleground without the patient voice present.

These patients are ready to engage. They understand the therapy, its impact and the stakes. Linking them with organizations such as RAAP and others working on access and policy ensures that the people most affected are part of the conversation. That is how we make sure the innovation your teams deliver actually reaches the patients it was designed to help.

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